BRITISH MEDICAL JOURNAL

LONDON SATURDAY FEBRUARY 22 1958

# TRIALS OF AN ASIAN INFLUENZA VACCINE

## FOURTH PROGRESS REPORT TO THE MEDICAL RESEARCH COUNCIL BY ITS COMMITTEE ON INFLUENZA AND OTHER RESPIRATORY VIRUS VACCINES*

Early in May, 1957, reports were received in this country of the occurrence of epidemic influenza in Japan, Hong Kong, and Singapore. It was subsequently ascertained that the epidemic had made its first appearance in South-Western China in February. Laboratory investigations at the World Influenza Centre, Mill Hill, London, the International Influenza Centre for the Americas, Montgomery, Alabama, the Walter Reed Army Institute of Research, U.S.A., and the Walter and Eliza Hall Institute, Melbourne, quickly showed that the causal virus was a new variant of virus A unrelated to all previously isolated strains. In these circumstances it was almost certain that this "Asian" influenza would spread from the Far East to this country. An opportunity was thereby presented to carry out serological and clinical trials of a vaccine made from the virus of this new type.

### I. THE SEROLOGICAL TRIAL

*The Vaccines.*—With the object of establishing the minimum strength of haemagglutinating units necessary to give an adequate antibody response, four saline vaccines were prepared by Dr. F. Himmelweit of the Wright–Fleming Institute of Microbiology. The methods of preparation were similar to those described in previous reports (M.R.C., 1953, 1955, 1957), the vaccines being made from the egg-adapted line of the Asian strain A/Singapore/1/57. Concentration from the original allantoic fluids provided a vaccine A of 20,000 haemagglutinating units† per dose. This was then diluted to give three vaccines of lesser strength. Thus the four vaccines employed were:

Vaccine A: 20,000 H.U. per dose
" B: Two-thirds of A, about 14,000 H.U. per dose
" C: One-third of A, " 7,000 " " "
" D: One-sixth of A, " 3,500 " " "

The haemagglutinating units of virus were in each vaccine adsorbed on to 10 mg. of aluminium phosphate per dose, and the dose in each was 1 ml., inoculated deep subcutaneously into the upper arm.

*Organization of the Trial.*—The trial was carried out in two groups: (*a*) Army personnel at the R.A.M.C. Field Training Centre at Mytchett, Hants, and (*b*) Royal Air Force personnel at Lindholme, Finningley, and Bawtry. In each group about 60 volunteers were obtained, mostly young men. They were divided into four subgroups, each to receive one of the four vaccines. Two serum samples were collected from each volunteer, the first just before inoculation and the second three weeks later. In view, however, of the comparatively small antibody responses which were observed after one dose, it was decided to ascertain the effect of a second dose given three to four weeks after the first. This was done in all the volunteers remaining in the subgroups originally given vaccines A and C. The sera were examined at the Wright–Fleming Institute, and the results confirmed at the World Influenza Centre, Mill Hill, and the Virus Laboratory at Lodge Moor, Sheffield.

#### Results

Table I shows the responses, by the haemagglutination-inhibition test, three weeks after one dose of the various vaccines. The most marked feature is the low antibody rises obtained with all four—although, except with the lowest strength of vaccine D, there were a few individuals who gave surprisingly good responses. These generally low antibody rises are not necessarily attributable to the virus being a poor antigen. They may be due to lack of any previous experience of the virus in the population or be associated with certain biological characteristics of the new strain predominantly due to its high sensitivity to non-specific inhibiting factors in the sera. This sensitivity necessitated treatment of the sera with cholera enzyme, which may reduce the antibody level to some degree.

TABLE I.—*Haemagglutination-inhibition Titres Observed Three Weeks After Primary Inoculation with Asian Influenza Vaccine of Different Strengths**

| Titre | Vaccine A 20,000 H.U. per Dose | Vaccine B 14,000 H.U. per Dose | Vaccine C 7,000 H.U. per Dose | Vaccine D 3,500 H.U. per Dose |
|---|---|---|---|---|
| 10 or under | 9 | 15 | 13 | 11 |
| 12·5–17·5 | 9 | 8 | 6 | 6 |
| 20–50 | 13 | 3 | 6 | 8 |
| 60–120 | 3 | 2 | 4 | — |
| Total | 34 | 28 | 29 | 25 |
| Geometric mean titre | 14·9 | 7·6 | 9·8 | 7·2 |

* The H.I. titres prior to inoculation were in all cases less than 5.

*Members of the Committee: Professor C. H. Stuart-Harris (chairman), Dr. C. H. Andrewes, F.R.S., Dr. B. E. Andrews, Brigadier G. T. L. Archer, Dr. W. H. Bradley, Brigadier P. J. L. Capon, Surgeon Captain T. L. Cleave, Professor R. Cruickshank, Dr. J. J. O'Dwyer, Professor A. Bradford Hill, F.R.S., Dr. F. Himmelweit, Dr. A. Isaacs, Dr. F. O. MacCallum, Dr. J. C. McDonald, Dr. W. J. Martin, Dr. A. T. Roden, Dr. I. N. Sutherland, Professor Wilson Smith, F.R.S., Air Commodore J. S. Wilson, Brigadier A. E. Richmond (secretary).

†The equivalence between haemagglutinating units and the C.C.A. units used in American reports is at present being investigated. Based on preliminary inquiries by means of direct comparisons of the two methods and comparison of stock vaccines with American standard preparations kindly supplied by Dr. Roderick Murray, National Institutes of Health, Bethesda, U.S.A., 1 C.C.A. unit seems to be equivalent to between 25 and 40 haemagglutinating units. Further investigations are being carried out to enable a more precise figure of equivalence to be reached.

The geometric mean titres do not differ significantly between vaccines B, C, and D, while the difference between vaccine A and vaccines B, C, and D combined is just significant ($t=2.32$ with 114 d.f., $0.02<p<0.05$).

The complement-fixation test on 34 paired samples (carried out at the Central P.H. Laboratory, Colindale) demonstrated a better response than the H.I. test.

The results of a second dose of vaccines A and C, given three to four weeks subsequent to the first dose, are shown in Table II. It will be seen that the boosting effects of the second dose were considerable and that there was little to choose between the two vaccines in this respect.

TABLE II.—*Haemagglutination-inhibition Titres Observed About Three Weeks After First and Second Doses of Asian Influenza Vaccines, the Second Dose Given Three to Four Weeks After the First*

| Titre | Vaccine A 20,000 H.U. per Dose | | Vaccine C 7,000 H.U. per Dose | |
|---|---|---|---|---|
| | After First Dose | After Second Dose | After First Dose | After Second Dose |
| Under 20 | 13 | — | 16 | 1 |
| 20–50 | 7 | 5 | 3 | 8 |
| 60–120 | — | 13 | 2 | 11 |
| 121–240 | — | 2 | — | 1 |
| Total | 20 | 20 | 21 | 21 |
| Geometric mean titre | 8·8 | 77·7 | 4·2 | 56·5 |

## II. FIELD TRIALS

It was impossible to complete these serological trials and, consequently, to decide upon the vaccines, doses, etc., to be employed in the field trials until the end of August, 1957. Meanwhile it was known that cases of the Asian type of influenza had been imported and there had been a few localized outbreaks. The first evidence of the epidemic spread of the disease was in schools in Colne (Lancs) in the week ending August 24 and at the same time in Sheffield (Yorks). From then onwards the epidemic spread rapidly, reaching its peak earlier in the north of the country than in the south. Maximum incidence in the East and West Ridings of Yorkshire was in the week ending September 24 and in the Northern and North-Western regions and Wales in the week ending October 1. In the Midland regions the peak was reached in the week ending October 8, and in the Eastern, London, and more southerly regions in the week ending October 15. The recession subsequent to these weeks of maxima was gradual, but by mid-November the prevalence was low compared with that of the peak period. In view of this early arrival of the epidemic the field trials, originally planned for the late autumn, had to be expedited to the utmost extent. However, while it was possible to hasten the start in some of the centres, little could be done with regard to the public schools and teachers training colleges, which did not reopen for the Michaelmas term until after mid-September. Furthermore, in a number of these centres the epidemic began so early in the term that no trial was possible.

*The Centres.*—Ultimately the centres in four main groups which took part were as follows:

A. *Public Schools.*—Canford School, Durham School, Epsom College, Haileybury and Imperial Service College, St. Lawrence College, Marlborough College, Stonyhurst School, Trent College.

B. *Teachers Training Colleges.*—Bedford College of Physical Education, Dartford College of Physical Education, the City of Leeds, Didsbury, Trent Park, and Westminster Training Colleges.

C. *Miscellaneous Centres.*—Ministry of Health (London), Ministry of Pensions and National Insurance (Newcastle), London County Council Ambulance Service, London Transport Executive (Chiswick), H.M. Dockyard Portsmouth, Sheffield University, Messrs. Boots Pure Drug Company Limited, Nottingham.

D. *Chronic Bronchitics.*—Approximately 2,500 volunteers from chest clinics in England, Wales, and Scotland in a special trial organized in association with the Research Committee of the British Tuberculosis Association.

The trials in all these centres were planned to continue until the spring of 1958. This present report deals only with the period from their start until the end of November, and is limited to those centres from which sufficient information is already available for study. Thus two schools, one teachers training college, and the whole of group D are excluded.

*Procedure.*—As in the previous trials (M.R.C., 1953, 1957), volunteers for vaccination were allotted in random order to the different vaccines under trial, and they, as well as the medical practitioners subsequently diagnosing their illnesses, were kept in ignorance of the particular vaccine that had been given to any recipient. In the diagnosis of influenza reliance had to be placed mainly upon clinical assessment. On the other hand, the Public Health Laboratory Service, and certain other laboratories, were active in laboratory diagnosis and confirmed the presence of the Asian strain in a proportion of the cases occurring in some trial centres, particularly in the public schools.

### The Vaccines

The vaccines against the Asian virus were based on the results of the serological trials, and the aim of the field trial was to study the relative values of the following procedures:

(1) Two doses, each of about 7,000 haemagglutinating units
(2) One dose of about 7,000 haemagglutinating units
(3) One " " 20,000 " "

In addition a polyvalent vaccine from the older strains was used to find out whether a vaccine containing these strains had any preventive effect. A vaccine of the influenza B type was used as a control.

The following gives in detail the vaccines made at the Wright–Fleming Institute of Microbiology, and employed in the different groups.

A. *Public Schools.*—(1) An Asian type saline vaccine from the strain A/Singapore/1/57, with 20,000 H.U. per dose of 1 ml. and 10 mg. of aluminium phosphate, to be given in one dose. (2) A polyvalent saline influenza A vaccine containing equal proportions of Swine PR.8 and FM.1 with 20,000 H.U. per dose of 1 ml. and 10 mg. of aluminium phosphate, to be given in one dose. (3) An influenza B vaccine (1954) with 20,000 H.U. per dose of 1 ml. and 10 mg. of aluminium phosphate, to be given in one dose.

B. *Teachers Training Colleges*, and C. *Miscellaneous Centres.*—(1) An Asian type saline vaccine from the strain A/Singapore/1/57 with approximately 7,000 H.U. per dose of 1 ml. and 10 mg. of aluminium phosphate, to be given in two such doses, the second to be given 28 days after the first. (2) The same as (1) but limited to one dose only. (3) An influenza B vaccine as in A (3) above.

These vaccines have been given to 3,093 persons in the trials here described. Soreness of the arm and a slight malaise for 24–36 hours have been not unusual, but no serious reactions have so far been noted.

### Influenza Prevalence in Relation to Inoculation Dates in the Areas and Communities Concerned in the Trials

Before examining the results it is necessary to consider periods in which Asian influenza was prevalent in relation to dates of inoculation.

For the public schools comprising group A detailed information is given in the note accompanying Table III.

In the teachers training colleges of group B the inoculation dates varied from September 16 to 30, with the large majority between September 23 and 25. In every centre save one in this group the influenza epidemic started shortly before the inoculations were given, while in the one exception it began the day after.

TABLE III.—*Public Schools. Influenza Cases in Inoculated Boys According to the Length of Time Elapsing after Inoculation*

| Vaccine | School | No. of Boys Inoculated | No. of Cases Occurring | | | Cases Expressed as a Percentage of those Inoculated in Each Vaccine Group | | |
|---|---|---|---|---|---|---|---|---|
| | | | Days after Inoculation | | | Days after Inoculation | | |
| | | | 1–8 | 9–15 | 16 and Over | 1–8 | 9–15 | 16 and Over |
| Asian | Canford School | 75 | 2 | 7 | — | 2·7% | 9·3% | — |
| | Epsom College | 51 | 15 | 2 | — | 29·4% | 3·9% | — |
| | Haileybury and I.S. College | 139 | 23 | 10 | 2 | 16·5% | 7·2% | 1·4% |
| | Marlborough College | 97 | 51 | 10 | — | 52·6% | 10·3% | — |
| | St. Lawrence College | 42 | 4 | 4 | 3 | 9·5% | 9·5% | 7·1% |
| | Trent College | 64 | 36 | — | — | 56·3% | — | — |
| | Total (excluding Trent College) | 404 | 95 | 33 | 5 | 23·4% | 8·2% | 1·2% |
| Polyvalent Virus A (Non-Asian) | Canford School | 70 | 3 | 19 | 5 | 4·3% | 27·1% | 7·1% |
| | Epsom College | 62 | 16 | 17 | 1 | 25·8% | 27·4% | 1·6% |
| | Haileybury and I.S. College | 140 | 27 | 33 | 5 | 19·3% | 23·6% | 3·6% |
| | Marlborough College | 103 | 48 | 25 | — | 46·6% | 24·3% | — |
| | St. Lawrence College | 62 | 7 | 13 | 3 | 11·3% | 21·0% | 4·8% |
| | Trent College | 71 | 52 | 2 | — | 73·2% | 2·8% | — |
| | Total (excluding Treat College) | 437 | 101 | 107 | 14 | 23·1% | 24·5% | 3·2% |
| Control Virus B | Canford School | 73 | 4 | 23 | 4 | 5·5% | 31·5% | 5·5% |
| | Epsom College | 56 | 14 | 7 | — | 25·0% | 12·5% | — |
| | Haileybury and I.S. College | 143 | 18 | 43 | 5 | 12·6% | 30·1% | 3·5% |
| | Marlborough College | 100 | 55 | 21 | — | 55·0% | 21·0% | — |
| | St. Lawrence College | 57 | 3 | 12 | 7 | 5·3% | 21·1% | 12·3% |
| | Trent College | 62 | 43 | — | — | 69·4% | — | — |
| | Total (excluding Trent College) | 429 | 93 | 106 | 16 | 21·7% | 24·7% | 3·7% |

*Canford School*: Epidemic began October 5, ended October 19; whole school attack rate about 46%. Inoculations September 27 and 28 with one or two boys a few days later.
*Epsom College*: Epidemic began September 27, ended October 13; whole school attack rate about 61%. Inoculations September 28.
*Haileybury and I.S.C.*: Epidemic began about September 21, ended about October 16; whole school attack rate about 44%. Inoculations September 23, 24, 26, 27.
*Marlborough*: Epidemic began September 22, ended October 4; whole school attack rate about 80%. Inoculations September 27.
*St. Lawrence College* (senior school): Epidemic began October 1, ended October 23; whole school attack rate about 42%. Inoculations mainly September 29 and October 1, but some October 13. Through a clerical error, not affecting the random allocation, rather fewer boys were given the Asian vaccine.
*Trent College*: Epidemic began September 25, ended October 6; whole school attack rate about 79%. Inoculations September 27 and 28. Excluded from the total, since the epidemic was over within the eight days after inoculations.

It should be added that volunteers who before inoculation had succumbed to an attack of Asian influenza were automatically excluded from the trial.

In the miscellaneous centres comprising group C most of the inoculations were given between September 10 and 19. In the Ministry of Health some inoculations were delayed till late September and early October, while in the London Transport Executive establishment at Chiswick none were given until the second week in October. At Sheffield University, while volunteers amongst the resident staff were inoculated in the last fortnight of September, inoculation of the students was not done until between October 1 and 18.

In the London area influenza was particularly prevalent from about September 23 to November 2, and in Portsmouth the situation was much the same. In Sheffield, Newcastle, and Nottingham, the epidemic had begun two to three weeks earlier. In Sheffield University students, as distinct from resident staff, the epidemic began after the students had rejoined, and the peak of the epidemic in them was reached by October 15, a month later than in the resident staff.

In general it may be stated that in these centres influenza was definitely prevalent for some time subsequent to the inoculations. On the other hand, as a result of this overlap between inoculations and epidemicity in various centres, it has been impossible to measure the effect of two doses as compared with one. Many of these second doses were given within or subsequent to the recession of the epidemics. Under these circumstances the two-dose and single-dose vaccines were to all intents and purposes the same vaccine, and they have therefore been combined in presenting the results.

## Results

To take account of the fact that the inoculations were not complete before the epidemics began, the results in each centre have been analysed for different intervals of time following the inoculations. Thus Tables III, IV, and V show the attack rates falling upon the different vaccinated groups within the first eight days of their vaccination and at later intervals.

### A. Public Schools (Table III)

The figures for all schools combined show very clearly that in the first eight days after inoculation there was practically no difference at all between the three vaccinated groups in the proportions contracting influenza, the attack rates being 23.4%, 23.1%, and 21.7%. On the other hand, within 9 to 15 days after inoculation there is one pronounced difference between the three groups, since the attack rate was only 8.2% of those given the Asian vaccine compared with 24.5% and 24.7% in the other two groups given non-Asian vaccine. This advantage was maintained in the 16 days and over period, though by then the actual number of cases occurring was small.

Within the individual schools the same trend was consistently apparent (with the exception of Trent College, in which the epidemic came to an end within eight days). During days 9–15 the boys in the non-Asian vaccine groups in Epsom College, Haileybury and Imperial Service College, and Canford School had attack rates from influenza three times or more greater than the boys in the Asian vaccine group. In Marlborough and St. Lawrence Colleges the attack rate in the non-Asian vaccine group was approximately twice that of the Asian vaccine group. There was no evidence that the polyvalent non-Asian virus A vaccine exerted any preventive effect, since the attack rates with it and the virus B vaccine are remarkably similar.

If the figures are looked at in a slightly different way there were 309 boys who were inoculated with the Asian vaccine, 336 inoculated with the polyvalent virus A vaccine, and 336 inoculated with the virus B vaccine who had not been attacked by influenza within the first eight days after their inoculation. The numbers who succumbed after eight days were 38, 121, and 122, or only 12%, in those given the Asian vaccine, compared with 36% in each of the other two groups. In other words, the protection given appears to have been of the order of 67%.

### B. Teachers Training Colleges (Table IV)

The number of volunteers inoculated in these centres was only 318, and the centres have therefore been amalgamated.

Of the 62 cases of influenza reported, 44 occurred within the first eight days after inoculation. In this period the attack rates of those inoculated with Asian vaccine and the control vaccine were very similar—namely, 14.8% and 11.8% respectively. On the other hand, subsequent to the eighth day the attack rates were 2.8% in those who received the Asian vaccine and 11.7% in those given the virus B vaccine. The advantage to the former group is significant, and gives (on these small figures) a protective ratio of 75%.

TABLE IV.—*Teachers Training Colleges. Influenza Cases in Inoculated Students in Five Centres According to the Length of Time Elapsing After Inoculation*

| Vaccine | No. of Students Inoculated | No. of Cases Occurring | | | Cases Expressed as a Percentage of those Inoculated in Each Vaccine Group | | |
|---|---|---|---|---|---|---|---|
| | | Days after Inoculation | | | Days after Inoculation | | |
| | | 1–8 | 9–15 | 16 and Over | 1–8 | 9–15 | 16 and Over |
| Asian | 216 | 32 | 4 | 2 | 14·8% | 1·9% | 0·9% |
| Control virus B | 102 | 12 | 8 | 4 | 11·8% | 7·8% | 3·9% |

### C. Miscellaneous Centres (Table V)

Up to 15 days after inoculation cases of influenza and of other respiratory infections were few in number and did not differ significantly between the two vaccinated groups. On the other hand, from 16 days or more after inoculation, when the number of cases sharply increased under both diagnoses, 10.3% of those given the control virus B vaccine contracted influenza compared with 4.9% of those inoculated with the Asian type, the difference being statistically significant. As regards other respiratory infections there was no significant difference, the figures being 4.8% and 6.0% respectively. The protective ratio when influenza appears to have become prevalent is 52%.

TABLE V.—*Miscellaneous Centres. Absences from Work Reported as Due to (a) Influenza; (b) Other Respiratory Infections in Seven Centres According to the Length of Time Elapsing After Inoculation*

| Vaccine | No. Inoculated | No. of Cases Occurring within Specified Intervals after Inoculation | | | | | |
|---|---|---|---|---|---|---|---|
| | | 1–8 Days | | 9–15 Days | | 16 Days and Over | |
| | | No. | Rate | No. | Rate | No. | Rate |
| *(a) Influenza* | | | | | | | |
| Asian | 861 | 10 | 1·2% | 9 | 1·0% | 42 | 4·9% |
| Control virus B | 447 | 2 | 0·4% | 4 | 0·9% | 46 | 10·3% |
| *(b) Other Respiratory Infections* | | | | | | | |
| Asian | 861 | 9 | 1·0% | 5 | 0·6% | 41 | 4·8% |
| Control virus B | 447 | 2 | 0·4% | 2 | 0·4% | 27 | 6·0% |

## Discussion

The results obtained in these trials suggest that a very substantial protective effect was afforded by the Asian vaccine subsequent to the eighth day after its inoculation. The evidence from the public schools is particularly impressive, since the total number of volunteers was relatively large and the boys were under close observation. Laboratory investigations were carried out in a few individuals at most of them and confirmation of the cause of the epidemics was obtained. Particular attention may perhaps be given to Canford School, in which the epidemic did not begin until some days after the completion of inoculation. The attack rates during days 9–15 are very similar in the two non-Asian vaccine groups, 27.1 and 31.5%, whereas in the Asian vaccine group only 9.3% were attacked. The situation was similar in the 16-day-and-over period, though the actual number of cases was smaller. From these figures it seems legitimate to estimate a protection rate of not less than 66%. If the total figures for the schools are taken, there is a very similar picture.

The Asian vaccine on trial in the miscellaneous centres and teachers training colleges was only one third the strength in haemagglutinating units of the vaccine employed in the public schools. It is, however, difficult to make any precise comparison between these strengths, since extensive epidemics of Asian influenza comparable to those in the schools did not materialize in these two groups, and the numbers of absences reported as due to influenza were comparatively small. The results obtained from these two groups, however, support those obtained from the public schools.

## Summary

Serological trials were carried out in some 120 volunteers in Army and Royal Air Force units in July and August, 1957, to establish the optimum dosage and strength in haemagglutinating units to be recommended in a vaccine made from the Asian strain A/Singapore/1/57. Four vaccines were prepared with 20,000 and about 14,000, 7,000, and 3,500 H.U. per dose respectively. The antibody response to a single dose was low with each strength, though there was a somewhat greater response to the strongest. A second dose given three to four weeks later gave much greater antibody responses.

In field trials carried out in public schools, teachers training colleges, and other miscellaneous centres volunteers were allocated at random to an Asian influenza vaccine, a polyvalent virus A vaccine, or a virus B vaccine. Severe epidemics took place in the public schools, and, subsequent to eight days after inoculation with one dose, a very definite preventive effect was apparent in the Asian vaccine group. After that interval of time its attack rate fell to one-third of the rate observed in the other two groups. The equality in these other two groups suggests that no protection was conferred by the polyvalent virus A vaccine (though the young ages of the boys concerned may have been a factor in this). At a much lower epidemic level a similar protective effect was observed in the training colleges and other centres.

### Acknowledgments

Many have been concerned directly or indirectly in these trials, and without their help and co-operation little could have resulted. The Committee stresses the debt of gratitude it owes them.

Its very grateful thanks are due to all those in the miscellaneous centres, the Services, the public schools, and teachers training colleges who volunteered for inoculation in spite of the personal inconvenience frequently caused and who provided the essential human material for the trial.

The Committee's gratitude is also due to all those in the various centres, including the medical officers concerned, who were responsible for obtaining volunteers, for arranging inoculations, and for other necessary activities, and who with their subordinate staffs played a very important part.

At the same time the Committee is not forgetful of the help given by many general practitioners, particularly in those centres in which diagnosis lay in their hands.

The P.H.L.S. and certain other laboratories deserve special mention for their close co-operation, so freely given, and for their vital contribution to the trials.

The Committee wishes finally to express its appreciation of the work of the Virological Department of the Wright Fleming Institute, which was so intimately concerned with the preparation of the trial vaccines.

### REFERENCES

Medical Research Council Committee on Clinical Trials of Influenza Vaccine (1953). *Brit. med. J.*, **2**, 1173.
—— (1955). Ibid., **2**, 1229.
—— (1957). Ibid., **2**, 1.

# THE AUTUMN INFLUENZA OUTBREAK IN ENGLAND AND WALES

BY

**W. J. MARTIN, D.Sc., Ph.D.**

*Statistical Research Unit of the Medical Research Council, London School of Hygiene and Tropical Medicine*

The impression, gathered from various general sources, of the recent outbreak of influenza is that it first appeared in Yorkshire, spread almost immediately to the north and then more slowly to the south of the country, and that the northern section had the more severe experience. The attack rate, particularly in schools and closed communities, appears to have been very large, with a low fatality rate. It has been shown* that influenza epidemics are invariably accompanied by a rise in the number of deaths attributed to other causes, particularly to diseases of the respiratory and circulatory systems, and that the deaths from influenza account for only one-quarter to one-third of the increased mortality occurring in the epidemic period. It seemed of interest to examine the available data to see whether there were any indications of regional differences in size or severity of the epidemic.

TABLE I.—*Deaths and Notifications of Acute Pneumonia in the Great Towns*, 1957

| Week No. | Date | No. of Deaths | | | Notifications of Acute Pneumonia | Increases of 1957 over 1956 | | |
|---|---|---|---|---|---|---|---|---|
| | | All Causes | Pneumonia | Influenza | | All Causes Deaths | Pneumonia Deaths | Pneumonia Notifications |
| 35 | Aug. 31 | 4,474 | 144 | 2 | 101 | 105 | 0 | 18 |
| 36 | Sept. 7 | 4,689 | 177 | 8 | 125 | 33 | 19 | 21 |
| 37 | ,, 14 | 4,692 | 245 | 47 | 210 | 44 | 84 | 86 |
| 38 | ,, 21 | 5,211 | 273 | 121 | 447 | 651 | 121 | 352 |
| 39 | ,, 28 | 5,410 | 418 | 282 | 809 | 869 | 266 | 630 |
| 40 | Oct. 5 | 6,070 | 493 | 442 | 1,078 | 1,496 | 337 | 930 |
| 41 | ,, 12 | 6,761 | 572 | 591 | 1,226 | 1,869 | 380 | 1,065 |
| 42 | ,, 19 | 6,544 | 552 | 600 | 1,359 | 1,416 | 347 | 1,190 |
| 43 | ,, 26 | 6,263 | 507 | 396 | 1,059 | 1,457 | 345 | 859 |
| 44 | Nov. 2 | 5,706 | 406 | 263 | 782 | 464 | 207 | 598 |
| 45 | ,, 9 | 5,661 | 306 | 149 | 435 | 346 | 102 | 258 |
| 46 | ,, 16 | 5,779 | 328 | 102 | 365 | 280 | 92 | 140 |
| 47 | ,, 23 | 5,947 | 353 | 70 | 293 | 340 | 120 | 68 |
| 48 | ,, 30 | 6,248 | 338 | 84 | 294 | 335 | 39 | 38 |
| 49 | Dec. 7 | 6,999 | 468 | 88 | 390 | 1,077 | 142 | 63 |

Although the outbreak was unusual in time of appearance the mortality was not exceptional. The number of deaths attributed to influenza in the great towns in the 11-weeks period (September 14 to November 23) centred on the week of the maximum was 3,063 compared with 2,844 and 7,752 in the spring outbreaks of 1953 and 1951, the previous two influenza epidemics. The rise in the influenza mortality can, at present, be shown only from the data of the great towns, which in recent years have contributed about 55% of the deaths from all causes in the whole country. The deaths from all causes, influenza, and pneumonia, and the notifications of pneumonia in the great towns are shown in Table I.

Deaths from all causes and from pneumonia were at a maximum in week 41, and they were 1.4 and 3.0, respectively, times the number of deaths in the corresponding week of 1956. The maximum for influenza deaths and for the notifications of acute pneumonia occurred a week later. The number of notifications of pneumonia was 8.0 times the number in the same week of 1956, and only five deaths from influenza were registered in the 42nd week of 1956. During weeks 40–43 influenza accounted for 32.5% of the 6,238 deaths in excess of the 1956 total, and the excess of pneumonia deaths formed 22.6% of the rise in deaths.

The death rates from influenza in the great towns by region and week of registration are shown in Table II. It is clear that influenza first appeared in the north of the country, and in week 38 the three northern regions had 85% of the 121 deaths. The maximum occurred in week 40 in the East and West Ridings and the North-west, in the following week in the North, Midlands, and Wales, and in the week after in the remainder of the country. The lowest death rates were in London and the South-east Region and in the Eastern Region, with maximum rates of 19 and 21 respectively. The South-western towns had a very high rate of 62 per million in week 42 ; this was due to Bristol C.B., where 16 of the 38 deaths were registered. For the remaining regions the maximum rate ranged from 31 to 45. A regional comparison of the epidemic by means of deaths is not ideal, since the fatality rate may vary between areas and in time, and it is possible that the fatality rate was different in the areas first attacked and those attacked later. Moreover, the great towns form a varying proportion of the

TABLE II.—*Death Rates from Influenza Per Million in the Great Towns*

| Week | Date | North | East and West Ridings | North-west | North Midlands | Midlands | East | London and South-east | South | South-west | Wales |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 35 | Aug. 31 .. | — | 0·4 | 0·3 | — | — | — | — | — | — | — |
| 36 | Sept. 7 .. | — | 0·4 | 1 | 1 | 0·4 | 1 | — | — | — | — |
| 37 | ,, 14 .. | 3 | 6 | 4 | 2 | 3 | 1 | 0·5 | — | — | — |
| 38 | ,, 21 .. | 11 | 12 | 17 | 4 | 2 | 2 | 0·2 | 2 | — | 4 |
| 39 | ,, 28 .. | 21 | 28 | 31 | 12 | 10 | 3 | 2 | — | 8 | 16 |
| 40 | Oct. 5 .. | 30 | **31** | **42** | 26 | 22 | 6 | 5 | 10 | 16 | 20 |
| 41 | ,, 12 .. | **36** | 21 | 38 | **43** | **45** | 14 | 14 | 18 | 36 | **34** |
| 42 | ,, 19 .. | 30 | 17 | 29 | 37 | 43 | **21** | **19** | **31** | **62** | 19 |
| 43 | ,, 26 .. | 9 | 7 | 17 | 19 | 27 | 18 | 16 | 31 | 33 | 15 |
| 44 | Nov. 2 .. | 8 | 6 | 8 | 14 | 17 | 18 | 12 | 18 | 20 | 10 |
| 45 | ,, 9 .. | 3 | 2 | 5 | 7 | 7 | 10 | 7 | 13 | 15 | 6 |
| 46 | ,, 16 .. | 3 | 2 | 5 | 6 | 3 | 7 | 4 | 9 | 5 | 7 |
| 47 | ,, 23 .. | 3 | 2 | 3 | 4 | 2 | 3 | 3 | 6 | 5 | 4 |
| 48 | ,, 30 .. | 1 | 1 | 3 | 4 | 3 | 5 | 4 | 6 | 7 | 7 |
| 49 | Dec. 7 .. | 1 | 2 | 3 | 6 | 1 | 3 | 5 | 8 | 3 | 1 |

TABLE III.—*New Claims to Sickness in England and Wales Expressed as a Percentage of the Number in Week* 35

| Week | Date | England and Wales | North | East and West Ridings | North-west | North Midlands | Midlands | East | London South-east | South | South-west | Wales |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 35 | Aug. 31 .. | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 36 | Sept. 7 .. | 116 | 113 | 136 | 129 | 114 | 108 | 107 | 109 | 100 | 104 | 113 |
| 37 | ,, 14 .. | 145 | 148 | 200 | 175 | 136 | 121 | 122 | 119 | 113 | 112 | 149 |
| 38 | ,, 21 .. | 193 | 216 | 256 | 274 | 179 | 150 | 139 | 135 | 120 | 127 | 223 |
| 39 | ,, 28 .. | 356 | 453 | **463** | 545 | 341 | 290 | 217 | 205 | 182 | 202 | 431 |
| 40 | Oct. 5 .. | 436 | **550** | 450 | **612** | 463 | 434 | 333 | 295 | 284 | 329 | **459** |
| 41 | ,, 12 .. | **454** | 499 | 333 | 506 | **470** | **527** | 478 | 427 | 418 | 535 | 400 |
| 42 | ,, 19 .. | 436 | 357 | 237 | 347 | 405 | 473 | **591** | **573** | **584** | **700** | 318 |
| 43 | ,, 26 .. | 339 | 238 | 179 | 231 | 284 | 320 | 502 | 506 | 549 | 565 | 242 |
| 44 | Nov. 2 .. | 260 | 178 | 153 | 177 | 214 | 227 | 393 | 393 | 422 | 398 | 197 |
| 45 | ,, 9 .. | 192 | 145 | 131 | 144 | 164 | 162 | 276 | 274 | 284 | 260 | 160 |
| 46 | ,, 16 .. | 161 | 141 | 127 | 416 | 144 | 141 | 206 | 200 | 202 | 187 | 147 |
| 47 | ,, 23 .. | 160 | 142 | 129 | 158 | 148 | 147 | 187 | 187 | 193 | 187 | 151 |
| 48 | ,, 30 .. | 164 | 139 | 126 | 163 | 149 | 150 | 189 | 195 | 198 | 194 | 155 |
| 49 | Dec. 7 .. | 172 | 136 | 124 | 157 | 152 | 155 | 209 | 225 | 213 | 204 | 155 |

*Mortality in Influenza Years, *Med. Offr.*, 1952, **87**, 127.

population exposed to risk in the different regions—for example, in the region of East and West Ridings 56.3% of the population live in the large towns, while in the South-west Region the percentage is only 25.4. A more general picture of the amount of sickness experienced can, however, be obtained from the new claims to sickness benefit under the National Insurance Act. These claims, expressed as a percentage of the claims in week 35, are shown in Table III.

The week of the maximum and the order of occurrence agree with the distribution of the maximum deaths in Table II. The largest rises between week 35 and the week of the maximum were in the regions of the South-west, 700%, and the North-west, 612%, while the lowest were Wales, 459%, and the East and West Ridings, 463%. Table III is based on the population of working ages and excludes married women who elected not to be insured in their own right. The most important omission is the child population, which was severely attacked by influenza. An indirect estimate of the severity of the influenza epidemic in the whole population can be obtained from the notifications of acute pneumonia; Table I shows that there is a correlation between influenza mortality and pneumonia mortality and incidence. The notifications of acute pneumonia per million population are shown in Table IV.

TABLE IV.—*Notifications of Acute Pneumonia in England and Wales, 1957. Rates Per Million*

| Week | Date | North | East and West Ridings | North-west | North Midlands | Midlands | East | London and South-east | South | South-wes. | Wales | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 35 | Aug. 31 .. | 4 | 9 | 4 | 4 | 6 | 2 | 3 | 2 | 3 | 3 | 4 |
| 36 | Sept. 7 .. | 5 | 11 | 6 | 4 | 5 | 5 | 2 | 4 | 2 | 5 | 5 |
| 37 | ,, 14 .. | 7 | 21 | 12 | 7 | 4 | 5 | 4 | 2 | 5 | 7 | 7 |
| 38 | ,, 21 .. | 24 | 44 | 30 | 14 | 14 | 9 | 4 | 2 | 6 | 17 | 16 |
| 39 | ,, 28 .. | 38 | **94** | 50 | 31 | 23 | 13 | 10 | 9 | 12 | 41 | 31 |
| 40 | Oct. 5 .. | 70 | 88 | **67** | 43 | 39 | 45 | 17 | 12 | 22 | 33 | 42 |
| 41 | ,, 12 .. | **88** | 76 | 63 | 54 | **66** | 51 | 27 | 28 | 44 | **41** | 51 |
| 42 | ,, 19 .. | 53 | 59 | 46 | **57** | 61 | 59 | 42 | **45** | **64** | 41 | 51 |
| 43 | ,, 26 .. | 44 | 37 | 24 | 45 | 52 | 66 | **43** | 39 | 58 | 31 | 43 |
| 44 | Nov. 2 .. | 11 | 24 | 16 | 20 | 30 | **72** | 38 | 31 | 51 | 38 | 32 |
| 45 | ,, 9 .. | 9 | 13 | 11 | 16 | 13 | 40 | 18 | 18 | 20 | 11 | 17 |
| 46 | ,, 16 .. | 10 | 16 | 11 | 7 | 12 | 28 | 14 | 12 | 18 | 13 | 14 |
| 47 | ,, 23 .. | 12 | 18 | 9 | 10 | 12 | 19 | 8 | 8 | 13 | 11 | 11 |
| 48 | ,, 30 .. | 11 | 19 | 9 | 5 | 9 | 16 | 8 | 19 | 14 | 9 | 11 |
| 49 | Dec. 7 .. | 19 | 22 | 11 | 16 | 11 | 23 | 12 | 14 | 16 | 9 | 15 |

The peak incidence was reached earlier in the three northern regions than in the remainder of the country. The largest maxima were 94 per million in East and West Ridings and 88 in the Northern Region, and the lowest were 41 in Wales and 43 in London and the South-east. The somewhat different picture given by Table IV from that of Table III may be due to differences in severity of the attacks between regions.

From the above comparisons it seems that London and the South-east Region had a relatively light attack and the East, South, and Wales also had a more favourable experience than the remainder of the country. The South-west Region, with very high values for new claims to sickness, number of notifications of acute pneumonia, and mortality in the large towns, was the exception to the north/south distribution of incidence.

---

In proportion to its population, Northern Ireland was doing three times as much as Great Britain in the field of medical welfare, said Dr. J. OLIVER, of the Northern Ireland Ministry of Health and Local Government, at a meeting in Belfast last week. There were 2,000 more hospital beds in Northern Ireland than ten years ago and four completely new hospitals were under construction, which was something without parallel in the rest of the United Kingdom. The number of medical specialists in Belfast had increased 60% since 1948, and in the rest of Northern Ireland by 200%. Infant mortality had fallen from 106 per 1,000 live births in 1913 to 29 in 1956.

# SUDDEN DEATH DUE TO FULMINATING INFLUENZA

BY

**D. BRUCE NEILSON, M.B., Ch.B.**

*Clinical Laboratories, Victoria Infirmary, Glasgow*

It has been stated in both the lay and the medical press that the Asian influenza epidemic was mild in nature. Certainly the reports by Lim *et al.* (1957) and Guthrie *et al.* (1957) of the epidemics in Singapore and Kuwait recorded only two deaths; and Smith *et al.* (1957) stated that in Malaya deaths were few, and the mortality was certainly low among the cases from several general practices reported in the *Journal* of November 2, 1957 (p. 1057). In Britain, however, a considerable number of deaths attributed to influenza were notified. For example, in the six-weeks period ending October 19 2,083 deaths were reported from England and Wales. Although a major factor in many of these was probably underlying pulmonary or cardiovascular disease, nevertheless a certain percentage must have been due primarily to pulmonary complications of influenza, particularly to staphylococcal and pneumococcal pneumonia. It is pertinent to note that 8,338 cases of acute pneumonia were notified from England and Wales in October, 1957. This represents a weekly average of 2,084 as against 275 in October, 1956.

Roberts (1957) described nine cases of fatal fulminating influenza in a Glasgow hospital; a further three cases seen over a 10-day period are reported here. The devastatingly sudden and unexpected manner in which death occurred in all three cases, reminiscent of the 1918–20 epidemic, justifies placing them on record; in no case was there clinical evidence of severe illness, much less impending death. In Cases 1 and 2 the patients died at home and were examined at the instance of the Procurator Fiscal, Glasgow, and the third patient died in hospital.

## Case 1

A man aged 22 was found dead in bed at home early one morning approximately four hours after returning from a dance. On the day before his death he had felt slightly unwell and complained of pain in his neck. (This was found at necropsy to be due to a small furuncle on the lower jaw.) There was no relevant past history.

*Post-mortem Appearances.*—The body was that of a muscular, normally developed young man. The larynx, trachea, and main bronchi were intensely congested and contained some frothy blood-stained fluid. Numerous small petechial haemorrhages were evident on the pleural surfaces of the lungs, which were practically airless, grossly congested, and oedematous throughout; blood-stained frothy fluid exuded freely from the cut surface. All five lobes were an intense crimson, and both lower lobes were consolidated and so friable as to disintegrate on light finger-pressure. There was no free fluid in the pleural sacs. The heart showed no obvious abnormality apart from petechial haemorrhages over the pericardial surface. The abdominal viscera, particularly stomach and kidneys, were grossly congested. The gastric veins were greatly engorged, and appeared as though injected with indian ink. The kidneys were uniformly dark red, almost purplish. The brain was congested and oedematous.

## Case 2

A man of 36 had no past history of serious illness. Three weeks before his death he had an attack of "flu" which was not severe enough to necessitate a visit by his

doctor. A few days later he was back at work apparently completely recovered. On the morning of his death he was at business as usual and made no complaint. That afternoon, however, he developed pain and tightness in the chest and vomited several times. This attack passed off in a few hours but recurred early in the evening shortly after a meal. He went to the bathroom, where he was sick, and almost immediately afterwards, while still standing over the basin, he became rigid and dropped dead.

*Post-mortem Appearances.*—The body was that of a well-nourished, normally developed man. The internal appearances were strikingly similar to those of Case 1. The tracheobronchial tree was markedly congested and both lungs were haemorrhagic; the lower lobes were consolidated. Again the gastric veins were very congested and prominent, and the kidneys were dark red in colour.

### Case 3

This patient, a man aged 30, attended a chest clinic on November 8, 1957. He complained of slight breathlessness on exertion, of three months' duration. There was no history of a recent acute pulmonary episode. Examination revealed signs of bronchitis with bronchospasm; an *x*-ray film of the chest was reported on as showing "a residual segmentary consolidation of the mid-basal segment of the right lower lobe." He was accordingly admitted to Mearnskirk Hospital, Glasgow.

On the morning of November 9 he was examined by a physician, who found no signs in his chest, and a further *x*-ray film revealed no alteration in his condition. He remained well all day and was apyrexial. At 9.55 p.m. he was seen by the house-physician, to whom he stated that he "felt fine." A few minutes later he arose from bed, went to a sink and vomited a large amount of blood; almost immediately afterwards he collapsed and died. During his brief stay in hospital he received two injections of a combination of procaine penicillin and streptomycin sulphate.

*Post-mortem Appearances.*—The body was that of a well-nourished, normally developed man. The larynx was injected. The trachea and main bronchi were markedly congested and were filled with frothy fresh blood. Both lungs were an intense crimson, and on section frothy blood-stained fluid escaped freely from the cut surfaces of the upper lobes. The lower lobes were consolidated and extremely friable, the left being more haemorrhagic in appearance than the right; blood exuded from their cut surfaces. There was no free fluid in the pleural sacs, where numerous dense adhesions were present over both lung bases. The stomach contained a considerable quantity of altered blood. The mucosa was congested and the gastric veins were extremely prominent. There was no obvious ulceration, and a source of haemorrhage could not be found. The liver and kidneys were much congested. The heart showed no abnormality and the adrenals appeared normal.

### Histology and Bacteriology

*Histological Features.*—In all three cases the microscopical picture was essentially similar. The tracheae and main bronchi were intensely congested, the arterioles, venules, and capillaries being dilated and engorged. Slight submucosal oedema and round-cell infiltration were found. Most of the respiratory epithelium was intact and was covered in parts by a little fibrinous exudate. In a few areas superficial necrosis had occurred. The lungs showed widespread severe capillary congestion, and many of the alveoli were filled with albuminoid fluid. In the consolidated areas they were completely filled with blood and many of the alveolar walls had ruptured. The smaller bronchi and bronchioles contained some albuminoid fluid together with desquamated epithelial cells and a few red cells; in Case 3 abundant fresh blood was present. Examination of many sections of the lungs from all three cases failed to reveal any cellular reaction in the lung parenchyma; a few lymphocytes and pigment-laden macrophages were the only cells present within the alveoli apart from erythrocytes. No organisms were found in sections stained with Gram's stain.

*Bacteriological Examination.*—Swabs were taken from the bronchi and lungs in each case. On direct examination of smears moderate numbers of Gram-positive cocci and diplococci were seen in the material examined from Cases 1 and 2, but in Case 3 Gram-negative bacilli were predominant. The scantiness of leucocytes was a noticeable feature in all cases. Cultures in the first two cases yielded a heavy growth of pneumococci and alpha-type streptococci which were sensitive to penicillin, erythromycin, streptomycin, tetracycline, and chloramphenicol. A few coagulase-positive staphylococci were grown after 48 hours' incubation, and these were sensitive to tetracycline but insensitive to penicillin, chloramphenicol, and streptomycin. In the third case a moderate growth of a coliform organism was obtained. This bacillus was sensitive to chloramphenicol, tetracycline, and erythromycin but resistant to penicillin and streptomycin. *Haemophilus influenzae* was not isolated in any case.

### Discussion

Although no virological investigation was undertaken there can be little doubt that these cases are examples of fulminating influenza. The pathological changes conform to those observed during the 1918–20 pandemic and bear a striking resemblance to those reported by Roberts (1957). In my cases the most significant features are the paucity of clinical symptoms and signs, coupled with the dramatic suddenness of death, the age of the victims, and the negative bacteriological studies. All the patients described by Roberts initially had the usual "flu" symptoms—namely, fever, sore throat, and prostration. These were followed 24–48 hours later by a marked deterioration in their condition, as evidenced by cyanosis and severe dyspnoea, and culminated in death several hours later. On the other hand, in my cases no such signs of serious illness were manifest. One victim had been out dancing a few hours before his death and had felt only slightly "off colour" that day. Another experienced symptoms (pain and tightness in the chest with vomiting) for the short period of approximately six hours before he succumbed; he was ambulant and collapsed after vomiting. The third, who died in a similar fashion, had actually been talking to the house-physician a few minutes before he died. The doctor did not suspect that the patient was seriously ill, and examination of his chest, including *x*-ray earlier that day, had revealed nothing of note. This is astounding in view of the gross pathological changes seen at necropsy.

Coagulase-positive staphylococci have been incriminated in a number of influenzal deaths during this epidemic, including those reviewed by Roberts. In the present cases no cocci were seen in the tissue sections, and only a few colonies of the organisms could be grown after 48 hours' incubation; thus it would appear unlikely that the staphylococcus played any significant part in the disease process. It is also difficult to imagine a *Streptococcus viridans* causing such a fulminating infection, and it is probable that the coliform organism found in Case 3 was a post-mortem contaminant. The pneumococci present in the first two cases were not predominant on culture and did not evoke any inflammatory reaction.

It has been generally thought that the majority of deaths in an influenza epidemic uncomplicated by underlying disease were due to secondary invasion of the lung by pathogenic organisms and not primarily to the virus. Thus it was reasonably supposed that our modern armamentarium of broad-spectrum antibiotics would prevent widespread fatalities in any severe epidemic. The observations here suggest the startling possibility that the violent haemorrhagic reaction in the lungs may have been due mainly to the virus and not to pathogenic bacteria. The haemorrhage was so severe that the patients virtually drowned in their

own blood. If this is the case, then at present our only hope of preventing such an occurrence lies in active immunization. This should be considered in the light of a possible second wave to the epidemic where the strain of virus may well be enhanced in virulence. As in my cases, the majority of deaths reported in this epidemic occurred in that intermediate group of people between the very young and the very old, and so it would seem desirable that this group should be the first to receive vaccination.

**Summary**

Three cases of sudden death in young men due to fulminating haemorrhagic influenzal pneumonia are described.

The gross pathological changes present in the lungs of these victims failed to produce correspondingly severe signs and symptoms.

The bacteriological and histological findings suggest that the haemorrhagic pneumonia may have been due primarily to the virus.

ADDENDUM.—Since this paper was written I have seen two further cases of precisely the same nature. The patients were males aged 51 and 24. The latter case is the subject of a medico-legal note on p. 469.

REFERENCES

Guthrie, J., Forsyth, D. M., and Montgomery, H. (1957). *Lancet*, **2**, 590.
Lim, K. A., Smith, A., Hale, J. H., and Glass, J. (1957). Ibid., **2**, 791.
Roberts, G. B. S. (1957). Ibid., **2**, 944.
Smith, C. E. G., Turner, L. H., and Halliwell, C. J. V. (1957). *Brit. med. J.*, **1**, 1412.

# THE INFLUENZA EPIDEMIC IN ABADAN

BY

**H. A. K. ROWLAND, D.M., M.R.C.P.Ed. D.T.M.&H.**

*From the National Iranian Oil Company Hospital, Abadan, Iran*

Abadan is a town of about 240,000 people, just under 143,000 of whom are cared for by the medical department of the National Iranian Oil Company. On the whole the climate is hot and dry, the maximum shade temperature varying from 110 to 122° F. (43.3 to 50° C.), and the maximum temperature in the sun rising to 179° F. (81.7° C.) during the period of the influenza epidemic.

All employed persons work in the oil refinery, there being 4,234 classified as "staff" and 26,351 as "labour." The respective figures for "dependants" are 10,351 and 101,716, the vast majority of whom are either wives or children under the age of 20 years. The standard of living of staff is higher than that of labour. Influenza is an unusual disease in Abadan, the great majority of the population at risk never having experienced the condition before.

For the purposes of this paper, the onset of the epidemic is taken as July 14, 1957. There were a few cases during the two weeks prior to that date, but they represent a minute fraction of the total number of persons affected by the illness.

Abadan can be reached by land, sea, and air. It is on the route of several international and national airlines, planes calling on their way to and from Europe, India, and the Far East. Land traffic into Abadan is comparatively small, but a large number of ships, both tankers and merchantmen, arrive from many parts of the world. During the 10 weeks prior to the onset of the epidemic, at least 28 tankers alone arrived in Abadan from ports further east where there was known to be influenza at the time of their departure. The first of these arrived from Singapore on May 1. It is therefore rather strange that the onset of the epidemic was delayed as long as it was.

The epidemic lasted nine weeks, the total number of cases being 44,921. The weekly figures are shown in Table I. Various measures, such as the closing of indoor cinemas and other gatherings, were taken, but no vaccine was used.

TABLE I.—*Weekly Totals*

| | | | | | |
|---|---|---|---|---|---|
| 1st week | 3,489 | 4th week | 10,210 | 7th week | 387 |
| 2nd ,, | 11,302 | 5th ,, | 4,488 | 8th ,, | 79 |
| 3rd ,, | 12,897 | 6th ,, | 2,042 | 9th ,, | 27 |

On the first day of the epidemic a large proportion of the patients were admitted to hospital, but thereafter only those whose condition was poor or who were suffering from complications were admitted, the remainder being treated as out-patients. Altogether 467 were admitted—412 with influenza and 55 with a complication.

When the patients were first seen the diagnosis was made on the presence of fever with one or more of the common symptoms. Details of the large number of patients treated in their own homes is not exact, and in many instances the total duration of the illness is not known. Treatment with aspirin, codeine, and cough mixtures was given to out-patients and in-patients suffering from uncomplicated influenza. Of the 44,483 whose initial illness was not treated in hospital, 55 were subsequently admitted suffering from a complication. Table II shows the number affected and the percentage incidence of the disease in children and adults in the staff and labour groups, from which it can be seen that labour was affected to a much greater degree than staff but that age made little difference.

TABLE II

| | | 0–19 Years | 20–60 Years | Total |
|---|---|---|---|---|
| Staff | No. affected | 1,093 | 1,780 | 2,873 |
| | Total population | 6,441 | 8,468 | 14,909 |
| | Percentage affected | 17·0 | 21·0 | 19·3 |
| Labour | No. affected | 25,502 | 16,546 | 42,048 |
| | Total population | 75,365 | 52,702 | 128,067 |
| | Percentage affected | 33·7 | 31·4 | 32·8 |
| Total | No. affected | 26,595 | 18,326 | 44,921 |
| | Total population | 81,806 | 61,170 | 142,976 |
| | Percentage affected | 32·5 | 29·9 | 31·4 |

### Patients Admitted Suffering from Uncomplicated Influenza

The 412 patients in this group were selected for admission because of the severity of the attack or for convenience in the case of nursing staff. There were 60 staff employed (29 males and 31 females), 127 labour employed (125 males and 2 females), 59 staff dependants (33 males and 26 females), and 166 labour dependants (69 males and 97 females). Twenty-seven patients subsequently developed a complication, all but one while in hospital. The latter patient was discharged, but a day or two later he was readmitted suffering from pneumonia. Table III shows the percentages of patients—children and adults, staff and

TABLE III.—*Percentage of Patients with Uncomplicated Influenza Admitted to Hospital*

| | 0–19 Years | 20–60 Years |
|---|---|---|
| Staff and dependants | 5·76 | 3·15 |
| Labour ,, ,, | 0·47 | 0·86 |

TABLE IV.—*Patients Admitted with Uncomplicated Influenza*

| | Duration of Fever Before Admission (Days) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Total duration of fever (days) { Max. | 9 | 9 | 12 | 8 | 9 | 13 | 10 | 13 | — | 12 | — | 14 |
| Total duration of fever (days) { Min. | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | — | 11 | — | 14 |
| Average total duration of fever (days) | 3·95 | 4·59 | 5·45 | 5·78 | 7·23 | 8·33 | 8·57 | 11·0 | — | 11·67 | — | 14 |
| Average duration of fever after admission (days) | 2·95 | 2·59 | 2·45 | 1·78 | 2·23 | 2·33 | 1·57 | 3·0 | — | 1·67 | — | 2·0 |
| No. of patients | 85 | 102 | 60 | 27 | 13 | 15 | 7 | 2 | — | 3 | — | 1 |
| Total duration of illness (days) { Max. | 17 | 17 | 21 | 14 | 16 | 24 | 15 | 20 | — | 30 | — | 29 |
| Total duration of illness (days) { Min. | 3 | 4 | 4 | 6 | 8 | 9 | 9 | 16 | — | 13 | — | 14 |
| Average total duration of illness (days) | 7·02 | 7·64 | 8·75 | 9·07 | 9·0 | 13·0 | 12·0 | 18·0 | — | 18·8 | — | 19·25 |
| No. of patients | 86 | 102 | 60 | 28 | 15 | 17 | 7 | 2 | — | 5 | — | 4 |
| Stay in hospital after fever subsided (days) { Max. | 12 | 13 | 14 | 10 | 8 | 10 | 8 | 11 | — | 18 | — | 3 |
| Stay in hospital after fever subsided (days) { Min. | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | — | 6 | — | 3 |
| Average stay after fever subsided (days) | 2·93 | 3·19 | 3·18 | 3·44 | 3·33 | 3·75 | 3·43 | 7·0 | — | 11·0 | — | 3 |
| No. of patients | 84 | 101 | 60 | 27 | 13 | 16 | 7 | 2 | — | 3 | — | 1 |

labour—who were suffering from an attack of uncomplicated influenza severe enough to warrant admission to hospital.

In the second to fifth weeks inclusive, during which time 85% of the total cases occurred, the percentage of patients suffering from uncomplicated influenza who were admitted varied between 0.37 and 0.72, suggesting that the severity of the attacks did not vary greatly as the epidemic progressed.

On admission patients gave a history of fever and other symptoms, the duration of which varied. Fever was complained of in 100%, headache in 74%, cough in 69%, generalized aching in 61%, sore throat in 35%, and vomiting in 13%. Haemoptysis was not a common occurrence during the acute attack, but was often seen during the two or three days after the fever had subsided, the blood being dark red or black.

The period of fever before admission varied from 1 to 12 days, and after admission from 1 to 9 days, while the overall duration of fever varied between 2 and 14 days. Table IV shows the relationship between the period of fever before admission, the average total duration of fever, and the average period of fever after admission to hospital. From this it can be seen that, while the total duration of fever increased with the period of fever prior to admission, the duration of fever after admission remained remarkably constant.

After the fever subsided the patients remained in hospital for a varying period of time. The middle part of Table IV relates the average stay in hospital after cessation of fever to the duration of fever before admission, and it can be seen that the latter had no effect on the duration of debility following the fall in temperature. From the lower part of Table IV it can be seen that the total duration of the illness increased steadily with the period of fever before admission.

## Complications

Altogether 82 patients (50 males, 32 females) suffering from influenza developed a complication. In 27 instances this developed in patients already admitted for the primary illness, the remaining 55 being admitted suffering from the complication, but giving a history of influenza immediately before its onset. The incidence of complications in the epidemic as a whole was 0.18%. Twelve patients were staff and 70 were labour. In the different groups the rates were: (*a*) staff 0–19 years, 0.92%; 20–60 years, 0.11%; (*b*) labour 0–19 years, 0.12%; 20–60 years, 0.24%.

Of the 412 patients admitted for severe influenza, 27 developed a complication, an incidence of 6.6%, whereas of the 44,509 who were not considered to be ill enough to warrant admission and who were treated as out-patients 55 were later admitted—an incidence of 0.12%.

The symptoms of the primary illness were similar to those in uncomplicated cases—namely, fever in 100%, cough in 78%, headache in 55%, generalized aching in 45%, sore throat in 16%, and vomiting in 16%. The incidence of complications varied from 0.1 to 0.34% over the first six weeks of the epidemic but in no definite manner.

Of the 82 patients, 35 developed bronchitis, 44 pneumonia, one jaundice, one otitis media, and one cerebral sinus thrombosis. The last-named patient and four suffering from pneumonia died in hospital, four of them having the complication on admission.

*Admitted with Uncomplicated Influenza.*—In six instances there was an afebrile period of one day before the onset of the complication, in a further six the temperature was normal for two days, and in one for three days. Six patients had been admitted on the first day of the primary illness, 11 on the second, four on the third, and four on the fourth to eighth days, while in two instances the day of onset was not known. Of these 27 patients, 15 developed bronchitis, 11 pneumonia, and one otitis media.

*Admitted Suffering from a Complication.*—In the majority of the 55 patients in this group it was not possible to discover whether there had been an afebrile period in the illness or the exact day on which the complication had started. The day of onset of the primary illness, however, was usually known.

TABLE V.—*Complications: Age and Sex Distribution*

| | 0–19 Years | | 20–60 Years | | Total |
|---|---|---|---|---|---|
| | M | F | M | F | |
| Bronchitis | 8 | 10 | 17 | — | 35 |
| Pneumonia | 8 | 11 | 17 | 8 | 44 |
| Jaundice | — | 1 | — | — | 1 |
| Otitis media | — | 1 | — | — | 1 |
| Cerebral sinus thrombosis | — | 1 | — | — | 1 |
| Total | 16 | 24 | 34 | 8 | 82 |
| Staff total | 4 | 6 | 2 | 0 | 12 |
| Labour total | 12 | 18 | 32 | 8 | 70 |

Table V shows the age and sex distribution of the complications. The patient who developed jaundice was a girl aged 7 years who was admitted to hospital on the seventh day of her illness, which had started with fever, headache, and generalized aching. This lasted for three days. She was then afebrile for two days, after which she again developed fever, headache, abdominal pain, and vomiting. On admission she looked ill, temperature 104° F. (40° C.), pulse 140, tongue coated, throat inflamed, spleen palpable, very obvious icterus of the skin and conjunctivae, and leucocytes 9,000/c.mm. The duration of the second period of fever was six days, during which time the jaundice gradually faded. She was discharged after 12 days in hospital.

## Treatment of Complications

Treatment for complications was started either on admission or when diagnosed in hospital. Except in some of the patients suffering from bronchitis and the patient with jaundice, this consisted of an antibiotic. Table VI records

TABLE VI.—*Drugs Used in Treatment*

| | Penicillin | Chloramphenicol | Chlortetracycline | Nil | Total Cases |
|---|---|---|---|---|---|
| Bronchitis .. | 7 | 19 | — | 9 | 35 |
| Pneumonia .. | 2 | 36 | 2 | — | 40 |
| Otitis media .. | — | 1 | — | — | 1 |
| Jaundice .. | — | — | — | 1 | 1 |
| Total .. | 9 | 56 | 2 | 10 | 77 |

the number of patients treated with the different drugs, the five patients who died being excluded. Penicillin dosage varied from 3 million units in six days to 13 million units in 16 days, and that of chloramphenicol from 3 g. in three days to 24 g. in eight days. In 69 of the patients suffering from bronchitis or pneumonia, the exact duration of the fever following onset of treatment was known, and the number of patients in the different groups is shown in Table VII. The total duration of the illness from onset

TABLE VII.—*Persistence of Fever*

| | Treatment | Duration of Fever After Start of Treatment (Days) | | | | | | | | Total Cases |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | |
| Bronchitis | No antibiotic .. | — | 1 | 3 | 1 | 2 | — | 1 | — | 8 |
| | Penicillin .. | 2 | 2 | — | 1 | 1 | — | — | — | 6 |
| | Chloramphenicol | 3 | 6 | 6 | 2 | 2 | — | — | — | 19 |
| Pneumonia | Penicillin .. | 1 | — | — | — | 1 | — | — | — | 2 |
| | Chloramphenicol | 7 | 11 | 6 | 5 | 3 | 1 | — | 1 | 34 |
| | Total .. | 13 | 20 | 15 | 9 | 9 | 1 | 1 | 1 | 69 |

TABLE VIII.—*Duration of Illness*

| Complication | Admitted as: | Total Duration of Illness (Days) | | | | | | | | Total Cases |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 0–5 | 6–10 | 11–15 | 16–20 | 21–25 | 26–30 | 30+ | Unknown | |
| Bronchitis | Influenza .. | | 6 | 8 | | | | | 1 | 15 |
| | Complication | | 8 | 4 | 3 | 2 | | 1 | 2 | 20 |
| Pneumonia | Influenza .. | | 4 | 3 | 3 | 1 | | | | 11 |
| | Complication | 1 | 11 | 9 | 2 | 3 | 1 | 1 | 1 | 29 |
| Jaundice | Complication | — | — | — | 1 | — | — | — | — | 1 |
| Otitis media | Influenza .. | — | — | 1 | — | — | — | — | — | 1 |
| Totals | Influenza | | 10 | 12 | 3 | 1 | — | — | 1 | 27 |
| | Complication | 1 | 19 | 13 | 6 | 5 | 1 | 2 | 3 | 50 |
| | Both together | 1 | 29 | 25 | 9 | 6 | 1 | 2 | 4 | 77 |

of influenza to discharge from hospital after treatment of the complication varied greatly in different patients, and the numbers in the various groups are recorded in Table VIII.

## Deaths

*Patient 1.*—A girl aged 2½ years was admitted with a history of fever, non-productive cough, and abdominal pain for the previous seven days. The general condition was found to be very poor; temperature 104.2° F. (40.1° C.), pulse 120 and very weak; dyspnoeic, cyanosed, and with widespread bilateral crepitation in the lungs. Chloramphenicol was given intramuscularly, but the child died six hours after admission.

*Patient 2.*—A woman aged 45 was admitted with a history of fever, non-productive cough, abdominal pain, vomiting, and severe headache for the previous two weeks. Her general condition was poor; temperature 101° F. (38.3° C.), pulse 120, and evidence of bronchopneumonia. She was treated with chloramphenicol by mouth and later intramuscularly. Her condition remained about the same for the next five days, and she died six days after admission.

*Patient 3.*—A girl aged 2 years was admitted with a history of headache and fever for the previous seven days. Despite treatment with chloramphenicol, given because *H. influenzae* predominated on culture of the throat swab, her general condition deteriorated and she died of bronchopneumonia three days after admission. She was a staff dependant.

*Patient 4.*—A man aged 55 had influenza, from which he recovered. Four days later he again became ill, with headache, cough, fever, and abdominal pain. On examination he was dehydrated, fibrillating, and with widespread bilateral crepitations in the lungs. He was given chloramphenicol, 2 g. initially, followed by 1 g. intramuscularly six-hourly, but he gradually deteriorated, became cyanosed and severely dyspnoeic, and died seven days after admission.

*Patient 5.*—A girl aged 10 gave a history of fever, headache, cough, little sputum, and vomiting for an unknown period of time. On admission, treatment with chloramphenicol, 500 mg. six-hourly, was started, but two days later she became comatose and was found to have some neck stiffness, pin-point pupils, variable strabismus, and flaccid limbs; all reflexes were absent. The left plantar response was extensor, the right not elicited. There was marked bilateral papilloedema but no evidence of sepsis of the face, ears, or scalp. Lumbar puncture yielded a normal fluid under very high pressure, and a diagnosis of cerebral sinus thrombosis was made. Streptomycin was added to the chloramphenicol, now given intramuscularly, and the next day she was more alert and reacted quickly to painful stimuli, moving all four limbs, but the papilloedema was unaltered. 15 ml. of C.S.F. was removed, and the next day the temperature had fallen to 100° F. (37.8° C.) and she was able to obey simple commands. 10 ml. of C.S.F. was removed. All specimens of C.S.F. showed no abnormality other than raised pressure. On the following day she again became comatose, the temperature rose to 105° F. (40.6° C.), spasticity developed in all four limbs, and she died within a few hours. Post-mortem examination was refused by the parents.

## Discussion

Following a period of two weeks, during which time there were sporadic cases only, the epidemic was an explosive one, there being nearly 3,500 people affected during the first week and the figure rising to almost 13,000 during the third week. It is not possible to be certain of the source of infection, but it is most likely that it was ships arriving from ports where influenza was present. It is surprising that the epidemic did not start in Abadan much earlier, as at least 28 ships arrived from already infected ports during the previous 10 weeks.

Of the 143,000 people under consideration, 31.4% developed influenza. Labour was much more affected than staff in the ratio of 32.8 to 19.3. Staff children were a little less affected than staff adults, and labour children a little more than labour adults, but the differences were not very marked. It is possible that more crowded living conditions caused the higher incidence amongst labour.

Table III indicates that the percentage of patients admitted was much greater among staff than among labour. This difference cannot be explained on the availability of beds, because at no time during the epidemic were all beds filled. Male labourers may have tended to stay at work for financial reasons. Labour patients were admitted to the Isolation Hospital, whereas staff were admitted to the General Hospital. The Isolation Hospital is feared by the population in general—a fear dating from the days when smallpox and typhus were more prevalent, and perhaps from the fact that tuberculosis is treated there to-day. Nursing staff were treated in hospital rather than in the Nurses' Home. These considerations tend to reduce the apparent discrepancy in the severity of the attack in staff and labour, the impression being that little difference existed at all.

The patients who were admitted were obviously ill. The temperature was usually 103–104° F. (39.4–40° C.) and up to 106° F. (41.1° C.), especially in small children. It is not thought that heat disorder played a part, because, although it was a hot summer, the incidence of heat hyperpyrexia was lower than in previous years, both in the local population and in the ships' crews. Sore throat was present in 35% of patients. This was also found to be common in Singapore, though in Kuwait (McCreadie, 1957) it was unusual.

Table IV shows that the total duration of fever and of the illness as a whole increased with the period of fever before admission but that the period of fever after admission and the subsequent period of debility remained fairly constant at about two to three and three to four days respectively. The total duration of the illness was seven to nine days in the majority of patients admitted. Exact figures are not available for the large number of patients treated as out-patients, but the impression is that the duration was less than in those admitted to hospital.

Complications, mainly bronchitis and pneumonia, occurred in 0.18% of all patients, but were much more common in those who had been admitted because of a severe attack of influenza (6.6%) than in those whose primary illness did not warrant admission (0.12%). Those who developed the complication in hospital had not been ill for a longer than average period before admission, so that it would appear that it was the severity of the primary illness rather than its duration that was important. It might have been expected that labour, with a lower standard of living, would have been more prone to complications, but this was not the case. Staff as a whole had a complication rate of 0.42% and labour of 0.17%, the discrepancy being due to the high rate of 0.92% in staff under the age of 20. Males developed complications more often than females, the ratio being 50:32, and younger children more often than older children.

Because of the predominance of *H. influenzae* in sputum cultures, chloramphenicol was the antibiotic most used in the treatment of respiratory complications. The response to treatment was moderately good, the temperature reaching normal within five days in the vast majority. In the case of bronchitis this was so, whether an antibiotic was used or not. The total duration of the illness varied from one to three weeks with a few exceptions, and this was only slightly longer in those admitted suffering from the complication than in those in whom it developed in hospital.

The five patients who died were all in poor condition on admission. With the exception of the child who developed cerebral sinus thrombosis, all were admitted suffering from the complication and had been ill for one to two weeks before admission. The death rate in the epidemic was therefore about 1 in 9,000. Reports from other parts of the world have shown that the case fatality has varied greatly from place to place. In Malaya it was reported at about 1 in 40,000, and in West Pakistan at 1 in 46,000, whereas in the Philippines it was as high as 1 in 220. In Aden (Fawdry, 1957), the deaths attributable directly or indirectly to the influenza epidemic were estimated at about 200, a case fatality rate of 1 in 350. There seems to be no very good reason for the great difference in the mortality in Aden and Abadan, which have similar climates and similar standards of living.

Up to the time of writing, the diagnosis of pulmonary tuberculosis has been made for the first time in 14 patients who had recently suffered from influenza. The history was the same in them all—the cough did not clear up after the temperature had subsided. So far, a relapse of pulmonary tuberculosis in a person recently affected by influenza has not been encountered. It is interesting that the daily out-patient attendance for all conditions is higher now after the influenza epidemic than at the same time in previous years. This is partly due to the malaria epidemic in progress at present, but, even allowing for this, the attendances are greater than usual.

### Conclusions

The influenza epidemic in Abadan started suddenly on July 14, 1957, and involved 31.4% of the 143,000 persons associated with the National Iranian Oil Company. The lower-income groups were more affected than the higher, but there was little difference in the incidence or severity of the attack in the two sexes or at different ages.

The attack consisted of an acute febrile illness with marked constitutional upset, cough, and, quite frequently, a sore throat. Going to bed early in the illness shortened its duration but had little effect on the period of fever after hospitalization or on the subsequent period of debility. The attack was not as short as has been suggested from other reports, the average duration of the uncomplicated illness being seven to nine days in those whose condition warranted admission to hospital.

Complications were mainly bronchitis and pneumonia, the incidence being very much greater in those patients who had a severe attack of influenza. The overall incidence was 0.18%. The response to treatment was fairly prompt. The case fatality of the epidemic was 1 in 9,000, four of the five deaths occurring in patients admitted for the complication. All five were in poor condition or had been ill for one or two weeks before admission.

The epidemic has resulted in an increase in the general ill-health of the community, and several patients have subsequently been found to be suffering from pulmonary tuberculosis.

I am grateful to Dr. M. Rouhani, principal medical officer, National Iranian Oil Company Hospital, Abadan, Iran, for the facilities he made available and for his permission to publish this paper.

REFERENCES

Fawdry, A. L. (1957). *Lancet*, 2, 335.
McCreadie, D. W. A. (1957). *Brit. med. J.*, 2, 684.

## ROLE OF INSULIN IN ACUTE HYPOGLYCAEMIC ACTION OF TOLBUTAMIDE

BY

**J. A. WEAVER, M.D., M.R.C.P.**
*Eli Lilly Travelling Fellow of the Medical Research Council*

**T. E. PROUT, M.D.**
*Senior Fellow in Medicine, U.S. Public Health Service*

**G. W. SCOTT, M.D., M.R.C.P.**
*Fellow in Medicine*

AND

**S. P. ASPER, jun., M.D., F.A.C.P.**
*Associate Professor of Medicine*

*From the Department of Medicine, the Johns Hopkins University School of Medicine and the Johns Hopkins Hospital, Baltimore, Maryland*

The mode of action of the sulphonylureas* as hypoglycaemic agents is unknown. They are believed by some to act by increasing the amount or the effectiveness of insulin. Others believe that their effect is unlike and independent of insulin. Since much of the experimental work is contradictory, some of the experiments which clearly differentiate these opposing views need re-evaluation.

There is evidence, widely accepted, that insulin increases the uptake of glucose by tissues. This effect of insulin can be demonstrated *in vivo* by an increase in the difference between the arterial and venous glucose concentrations (A.-V. difference) in extremities, provided there is no change in peripheral blood flow, and *in vitro* by an increase in the glucose uptake of the isolated rat diaphragm. In studies of the effect of the sulphonylureas on arterial-venous blood-sugar differences an increase has been demonstrated by Goetz *et al.* (1956) but not by Purnell *et al.* (1956). Incubation of the rat dia-

*In this paper the term "sulphonylurea" refers to either 1-butyl-3-*p*-tolysulphonylurea (tolbutamide) or 1-butyl-3-sulphanilylurea (carbutamide), since these drugs are generally held to have similar metabolic effects.

phragm with a sulphonylurea *in vitro* caused no increase in glucose uptake (Cahill *et al.*, 1957). However, von Holt *et al.* (1957) have shown an increase in glycogen synthesis by the rat diaphragm after exposure of the diaphragm to the sera of animals treated with a sulphonylurea.

The purpose of this study has been a re-evaluation of A.-V. glucose differences in diabetic patients after a single oral dose of tolbutamide (1-butyl-3-*p*-tolysulphonylurea) and a simultaneous estimation of the insulin-like activity of the sera before and after tolbutamide administration. In addition, studies in rabbits have been made to determine the effect of tolbutamide on the rate of disappearance of insulin $^{131}$I from the plasma.

## Methods

*Patients.*—Ten patients with diabetes mellitus of recent onset, not controlled by diet, were studied. None had been previously treated with insulin. The ages ranged from 38 to 78 years and all were female. A single dose of 3 g. of tolbutamide was given orally after an overnight fast. Blood samples were drawn with minimal stasis from an antecubital vein at intervals during the next three hours. Capillary (arterial†) blood samples were taken from an ipsilateral finger puncture within two minutes after the venous sample. The patients were semirecumbent for one hour prior to study and remained at rest throughout. Capillary bloods drawn in duplicate and duplicate samples from the venous bloods were used for glucose estimation by the anthrone method (Roe, 1955). With known standards of glucose, it was shown that the average difference of the mean of duplicate estimations was 1.3±0.38%. The mean difference between duplicate samples of venous blood is 2.29%, and the mean difference for duplicate samples of arterial blood is 3.51%.

*Bio-assay of Insulin in Serum.*—A biological assay for insulin-like activity of the sera obtained prior to and at 140 minutes after administration of tolbutamide was carried out, using the rat hemi-diaphragm technique, as previously described (Scott *et al.*, 1957). The incubating fluid used was a salt solution buffered with bicarbonate (Gey and Gey, 1936) containing 250 mg./100 ml. of glucose. The solution was gassed with 90% oxygen and 10% carbon dioxide before incubation. Analyses of glucose concentrations were determined by the glucose-oxidase method (Teller, 1956; W. P. McCann, 1957, personal communication).

*Insulin $^{131}$I.*—A single injection of tolbutamide, 50 mg. per kg. body weight, was given intravenously to each of six rabbits in order to study the effect of tolbutamide on the rate of disappearance of insulin $^{131}$I. Insulin $^{131}$I with a specific activity of between 2.5 and 8.2 microcuries of $^{131}$I per microgram of insulin was injected intravenously into the rabbits from 17 to 20 minutes after injection of the tolbutamide. The disappearance rate of insulin $^{131}$I from the plasma was determined after separation of the insulin $^{131}$I by paper electrophoresis as described by Berson *et al.* (1956).

## Results

The arterial and venous blood-sugar values of the 10 diabetic patients are shown in Table I. Of the 10 patients studied by this method, eight showed a decrease in three hours of more than 25% in the venous glucose concentration. These patients have been regarded as responding to tolbutamide. A decrease of 30% of the blood sugar within a four-hour period following tolbutamide administration has been used by Williams and Henley (1957) to select responsive patients.

From the data in Table I the A.-V. differences were calculated. Zierler and Andres (1956) have shown that when the arterial glucose concentration is decreasing with time, the A.-V. difference shows a similar trend. Therefore the A.-V. differences have been divided by the arterial concentrations (A.). It appears that the factor A.-V./A. is a better index of peripheral glucose uptake under the condition of constant blood flow than the absolute A.-V. difference (Elrick *et al.*, 1955).

†Capillary blood glucose levels have been shown to be equivalent to arterial blood glucose levels (Foster, 1923).

TABLE I.—*Arterial and Venous Glucose Concentrations, in mg./100 ml. in Diabetic Patients Following 3 g. of Tolbutamide Orally*

| Case No. | Age | | Time in Minutes after Tolbutamide | | | | | | | % Fall at 180 Min. |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 0 | 20 | 40 | 60 | 100 | 140 | 180 | |
| 1 | 75 | A | 237 | 215 | 205 | 196 | 162 | 140 | 117 | 50·4 |
| | | V | 206 | 213 | 193 | 181 | 155 | 137 | 109 | 47·1 |
| 2 | 61 | A | 191 | 171 | 160 | 133 | 121 | 106 | 79 | 58·6 |
| | | V | 181 | 164 | 155 | 125 | 93 | 106 | 90 | 50·3 |
| 3 | 62 | A | 254 | 235 | 206 | 224 | 177 | 148 | 123 | 51·6 |
| | | V | 228 | 228 | 207 | 190 | 164 | 140 | 117 | 48·6 |
| 4 | 38 | A | 354 | 311 | 307 | 296 | 288 | 244 | 214 | 39·6 |
| | | V | 337 | 321 | 295 | 292 | 266 | 223 | 215 | 36·2 |
| 5 | 67 | A | 320 | 302 | 305 | 285 | 252 | 241 | 235 | 26·6 |
| | | V | 293 | 285 | 274 | 261 | 244 | 225 | 217 | 26·0 |
| 6 | 47 | A | 302 | 293 | 280 | 245 | 215 | 178 | 151 | 50·0 |
| | | V | 288 | 268 | 309 | 230 | 207 | 175 | 158 | 45·2 |
| 7 | 65 | A | 257 | 228 | 210 | 199 | 182 | 163 | 157 | 38·9 |
| | | V | 230 | 234 | 225 | — | 212 | 164 | 147 | 36·2 |
| 8 | 48 | A | 221 | 225 | 206 | 189 | 214 | 203 | 191 | 13·6 |
| | | V | 191 | 224 | 250 | 179 | 171 | 149 | 121 | 36·6 |
| 9 | 43 | A | 333 | 286 | 297 | 288 | 280 | 259 | 239 | 28·2 |
| | | V | 269 | 277 | 301 | 303 | 304 | 267 | 237 | 12·0 |
| 10 | 78 | A | 515 | 474 | 471 | 454 | 424 | 402 | 381 | 26·0 |
| | | V | 455 | 456 | 439 | 431 | 392 | 418 | 358 | 21·3 |

The mean A.-V./A. ratios with the standard deviation for each time interval throughout the study are shown in Table II. The values at zero time and at each of the times between 60 and 180 minutes show no significant difference when analysed by means of the t test ($0.2>P>0.1$). There is a negative A.-V./A. ratio at 40 minutes, but this is not significantly different from the value at the control time ($0.1>P>0.05$). The fact that 5 of the 10 patients had a negative A.-V. difference at 40 minutes appears to account for this mean negative result.

TABLE II.—*Mean Glucose Concentrations of Arterial and Venous Blood of 10 Diabetic Patients After Tolbutamide, Expressed as a Percentage of the Control, and the A.-V./A. Ratio at Each Time Interval*

| Time (Min.) | Mean A.-V./A. ±S.D. | Mean Arterial Blood Glucose, % of Control ±S.D. | Mean Venous Blood Glucose, % of Control ±S.D. |
|---|---|---|---|
| 0 | 0·101±0·046 | 100% | 100% |
| 20 | 0·027±0·033 | 92·3%±4·7 | 91·2%±12·0 |
| 40 | −0·010±0·096 | 88·2%±5·0 | 99·6%±13·7 |
| 60 | 0·055±0·055 | 83·2%±6·0 | 88·6%±11·8 |
| 100 | 0·051±0·116 | 76·7%±9·9 | 81·3%±16·1 |
| 140 | 0·043±0·088 | 68·8%±11·7 | 73·0%±13·7 |
| 180 | 0·062±0·118 | 61·7%±14·4 | 64·1%±12·8 |

The decrease in both the arterial and the venous blood sugars as a percentage of their respective initial levels is also shown in Table II. The decrement in the mean arterial sugar concentration is greater than that in the mean venous blood sugar for each time interval.

Fig. 1 shows the sensitivity of the bio-assay in which the rat-diaphragm procedure was used for standard solutions of insulin. The effect of the sera from each of the 10 patients on the glucose uptake of the rat diaphragms is shown in Table III. The results for each serum represent the mean of three diaphragm assays. The results have been expressed as the difference in glucose uptake by the rat hemi-diaphragm exposed to sera compared with that of the hemi-diaphragm not exposed to sera in mg. of glucose per g. of diaphragm per hour. Since some sera produce inhibition of the glucose uptake, conversion of the results into equivalent insulin-like activity is not possible. The sera obtained before tolbutamide administration increased the glucose uptake to an average of 0.28 mg. per g. per hour. The sera obtained at 140 minutes following tolbutamide produced an average increase

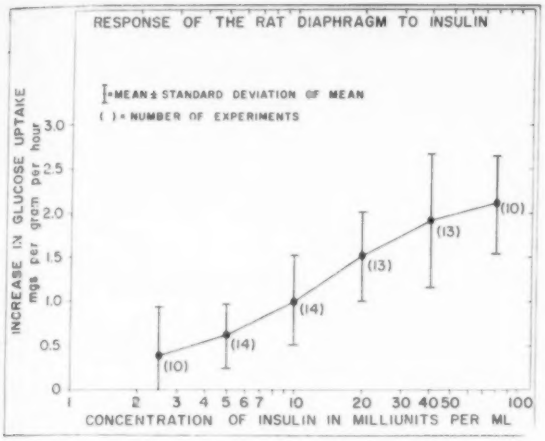



FIG. 1.—Bio-assay of insulin. The increase in the glucose uptake of the rat hemi-diaphragm exposed to various concentrations of insulin, above the glucose uptake of the hemi-diaphragm not exposed to insulin, is expressed in mg. per g. of diaphragm per hour. The mean for the number of duplicate determinations for each concentration, and the standard deviation of the mean, are shown. The slope calculated between 5 and 40 milliunits of insulin per ml. is 1.44 with a common standard deviation about means of 0.54 and index of precision of 0.37.

TABLE III.—*Effect of Sera of Diabetic Patients Before and at 140 Minutes After Tolbutamide. Each Figure Represents the Mean Increase in the Glucose Uptake of 3 Rat Hemi-diaphragms Exposed to Serum Above that of the Hemi-diaphragms Not Exposed to Serum, Expressed in mg. per Gramme per Hour. The Minus Values Represent an Inhibitory Effect of the Sera on the Glucose Uptake of the Hemi-diaphragm*

| Case No. | Before Tolbutamide | 140 Minutes after Tolbutamide |
|---|---|---|
| 1 | 0·09 | 0·48 |
| 2 | −0·08 | 0·42 |
| 3 | 0·35 | −0·13 |
| 4 | 0·22 | 0·66 |
| 5 | 0·08 | 0·52 |
| 6 | 0·66 | 0·92 |
| 7 | 0·23 | 0·95 |
| 8 | 1·10 | 1·30 |
| 9 | 0·72 | 0·49 |
| 10 | −0·53 | −0·34 |
| Mean ± S.E.M. | 0·28 ± 0·14 | 0·40 ± 0·17 |

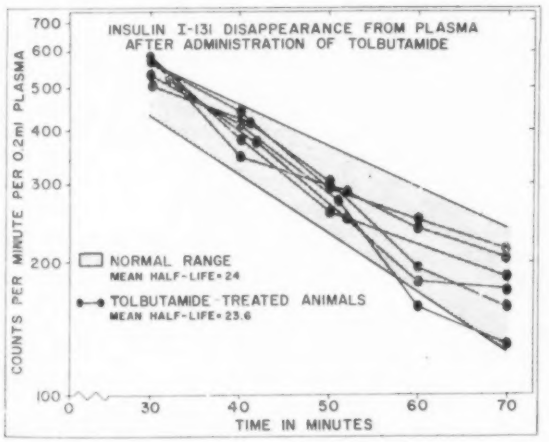



FIG. 2.—Comparison of the normal rate of disappearance of insulin $^{131}$I from plasma (mean half-life of 24 minutes) with that after intravenous injection of tolbutamide (mean half-life of 23.6 minutes). The normal range, shown by the shaded area, was derived from the results of a study of six untreated rabbits.

in the glucose uptake of 0.40 mg. per g. per hour. The mean difference is not significant as indicated by the t test ($P = 0.5$).

The effect of tolbutamide on the rate of disappearance of insulin $^{131}$I in rabbits is shown in Fig. 2. The first 30-minute period after injection of insulin $^{131}$I has not been charted as this represents the time of distribution of the insulin $^{131}$I into the available body space. The rate of disappearance of insulin $^{131}$I from the plasma following tolbutamide administration is within the range determined in six untreated rabbits.

The volume of distribution of insulin $^{131}$I was calculated for the untreated group by extrapolation of the rate of disappearance of insulin $^{131}$I to zero time. The theoretical concentration of insulin $^{131}$I per ml. of plasma thus obtained was divided into the total quantity of insulin $^{131}$I injected to obtain the theoretical volume of dilution. This calculation is based on the assumption that the rate of disappearance is constant throughout the period from 0 to 30 minutes. The apparent space of distribution of insulin $^{131}$I was found to be approximately 26% of body weight. This does not imply, however, that there is uniform distribution of insulin $^{131}$I throughout this space. The space of distribution of insulin $^{131}$I in the animals treated with tolbutamide was also approximately 26% of body weight.

## Discussion

It was originally suggested by Loubatières (1946) that the hypoglycaemic action of certain sulphonamide derivatives was insulin-dependent. This concept was based on the finding that these drugs were ineffective in the totally depancreatized animal. Moreover, it was shown that injections of small amounts of the drug into the pancreatic artery enhanced the hypoglycaemic response. The more recently synthesized sulphonylureas were also found to be ineffective in totally depancreatized animals (Houssay and Penhos, 1956) and in human subjects following pancreatectomy (Ogryzlo and Harrison, 1956). Administration of these drugs through the pancreatic artery enhanced the hypoglycaemic effect (Colwell *et al.*, 1956). After administration of a sulphonylurea drug to animals, there is an increase in the pancreatic islet tissue (Ashworth and Haist, 1956), and the insulin content of the pancreas is decreased for the first 24 to 48 hours (Root, 1957). Changes occurring in the granularity of the beta cells have been interpreted as evidence of insulin discharge (Lazarus and Volk, 1957).

Despite these experiments, which imply an insulin-dependent factor in the hypoglycaemic effect of the sulphonylureas, evidence for an increase in the effective level of insulin in peripheral tissue has not been clearly demonstrated. Purnell *et al.* (1956) failed to demonstrate evidence of an increase in the peripheral glucose uptake in either normal subjects or in diabetic patients after tolbutamide administration. In other experiments reported, tolbutamide increased the A.-V. glucose difference (Goetz *et al.*, 1956).

The A.-V. glucose difference can be used as an index of peripheral glucose uptake if the peripheral blood flow remains unchanged and the arterial glucose level is constant. An increase in peripheral glucose uptake could be present without change in the A.-V. glucose difference if peripheral blood flow were increased. Peripheral blood flow might be increased by adrenaline release associated with the trauma of the procedure or as a result of tolbutamide administration. Butterfield *et al.* (1957) studied blood flow in conjunction with determinations of capillary blood glucose after tolbutamide administration. No increase in peripheral blood flow was seen except in association with hypoglycaemia. None of the patients reported here, however, had a blood-sugar determination below 80 mg./100 ml. during the period of study. It is assumed, therefore, that neither the trauma of the procedure nor a direct effect of tolbutamide caused significant alteration in peripheral blood flow of the patients studied.

The decreasing arterial glucose concentration resulting from the hypoglycaemic effect of tolbutamide might have a direct effect on the A.-V. glucose difference. With a decreasing concentration of arterial blood glucose there is a simultaneous decrease in the A.-V. glucose difference (Zierler and Andres, 1956). Under these circumstances a relatively constant A.-V. glucose difference might be indicative of a more effective peripheral uptake of glucose, assuming no change in peripheral blood flow. However, in the studies reported here the A.-V. difference has been divided by the arterial glucose concentration. This was done to account for the effect of the decreasing arterial glucose concentration.

At 40 minutes following tolbutamide administration in the 10 diabetic patients the mean A.-V./A. ratio became negative. Comparison of the individual A.-V./A. ratios taken at 0 and 40 minutes revealed a decrease in the ratio in 8 of the 10 patients. In five of these eight patients there was a negative A.-V. difference at 40 minutes—that is, the venous glucose concentration was higher than the arterial. From studies of the A.-V. glucose differences in hypoglycaemia and hyperglycaemia, Somogyi (1948) stated that the arterial glucose concentration was always higher than the venous. However, negative A.-V. differences were found after insulin administration by Friedenson *et al.* (1928). Occasional negative A.-V. glucose differences were seen by Bell (1952), but were regarded as falling within the error of the analytical procedure. Zierler and Andres (1956) also noted negative A.-V. glucose differences.

Several of the negative differences found by us were small and could be interpreted as analytical errors. In some instances, however, large negative differences were found; these exceeded the analytical error of the procedure. In two patients throughout the period following tolbutamide administration, consistently greater concentrations of glucose were found in the venous blood than in the arterial blood. It is unlikely that these increased concentrations of glucose in the venous blood originated from within peripheral cells, since this possibility is not supported by present knowledge of glucose transfer across cell membranes. It could represent a diffusion of glucose from the extracellular fluid into the vascular compartment. This could occur only if the arterial glucose level had fallen below the concentration of the extracellular fluid in the limb. In the presence of a rapidly falling arterial glucose level such a phenomenon might occur. In these experiments the mean arterial glucose concentration decreased at each time interval more rapidly than the mean venous glucose concentration.

The limitations of the rat-diaphragm technique as a bioassay for insulin in serum are becoming increasingly recognized (Randle, 1956; Willebrands and Groen, 1956). For this reason, significance should be attached to the insulin-like activity in the sera of these patients as a group rather than as individuals. In view of the inherent difficulties, the possibility should be considered that this technique is not sensitive enough to detect an increase in endogenous insulin secretion. In the type of diabetic patient under study here, a maximum discharge of endogenous insulin of 1 unit per kg. is theoretically possible. This calculation is based on the quantity of insulin that is extractable at necropsy from the pancreas of such subjects (Wrenshall and Hamilton, 1957). The increase in serum insulin-like activity from the release of this insulin from the pancreas might vary widely, depending on the percentage of insulin released, the rate of insulin release, and the space of distribution of the insulin following release. The calculated increase in insulin in the serum could vary, therefore, from about 20 milliunits per ml. to less than 1 milliunit per ml. Since a fourfold increase in serum insulin-like activity can be distinguished by this assay, a mean increment of about 8 milliunits per ml. in these patients would have been statistically significant ($P. = 0.05$). There is no information, however, concerning the level of circulating insulin-like activity that is necessary to produce and maintain the decrease in blood glucose seen in these subjects. Although a definite conclusion cannot be reached, there is no positive evidence of an increased concentration of insulin-like activity in the serum following tolbutamide administration.

A further relationship of tolbutamide to insulin has been the finding of an inhibition of insulin degradation. This has been shown *in vitro* (Mirsky *et al.*, 1956), but could not be confirmed with a concentration of tolbutamide that might reasonably be expected to occur *in vivo* (Vaughan, 1956). Inhibition of insulin degradation *in vivo* (Mirsky *et al.*, 1956) has also been found, although this has not been confirmed by Cox *et al.* (1956), who used the technique of trichloroacetic acid precipitation.

A study of the fate of insulin $^{131}$I in diabetic subjects following tolbutamide administration has also been reported by Bolinger and Grady (1957). In their study the insulin $^{131}$I was determined after precipitation of plasma proteins with zinc hydroxide. An increase in the rate of insulin $^{131}$I disappearance from the plasma was shown following tolbutamide administration. This was interpreted as indicating an increase in uptake of insulin by the tissues rather than an increase in the degradation of insulin.

Berson *et al.* (1956) have shown that changes in the insulin molecule occur consequent to labelling with $^{131}$I. They also have demonstrated that the electrophoretic separation of insulin $^{131}$I from the plasma after its administration is a more accurate index of insulin metabolism than the technique of the trichloracetic acid precipitation of insulin; this has been confirmed by Scott *et al.* (1957).

The results of the study by Bolinger and Grady (1957), mentioned above, of the effect of tolbutamide on insulin $^{131}$I degradation are difficult to interpret in view of the failure to differentiate altered and unaltered insulin. Thus the slower rate of disappearance of the precipitable radioactivity prior to tolbutamide could be explained on the basis of the persistence of a larger fraction of altered insulin in the circulation. The theoretical concentration of labelled insulin at zero time which was calculated would be subject to the same error. In the studies reported here, in which the electrophoretic technique has been used to separate insulin $^{131}$I from the plasma, there was no effect of tolbutamide on insulin $^{131}$I disappearance or apparent space of distribution.

## Summary

Ten patients with diabetes mellitus of recent onset, not controlled by diet or previously treated with insulin, were each given a single dose of 3 g. of tolbutamide orally. Eight of these 10 patients showed a significant fall in the venous glucose concentration.

Studies on the difference between the arterial (A.) and venous (V.) glucose concentrations, expressed as A.-V./A., have shown no evidence of an increase in the uptake of glucose by the peripheral tissues in patients given tolbutamide.

Studies of insulin-like activity of serum, as assayed by the rat hemi-diaphragm method, have shown that there is no change in the insulin-like activity in the patients' serum before and after tolbutamide administration.

The rate of disappearance of intravenously administered insulin $^{131}$I from plasma was studied in normal rabbits by the electrophoretic technique. No difference in the rate of disappearance of insulin $^{131}$I was found following the injection intravenously of tolbutamide as compared with untreated animals.

These studies support the view that the hypoglycaemic action of tolbutamide is not produced by increasing the effective level of insulin.

This study was supported in part by grants from the Maryland Division, American Cancer Society, and the United States Public Health Service (Grant number AF-6051-C). We acknowledge with appreciation the technical assistance of Miss Judith Lebo. The tolbutamide used in this study was kindly supplied by the Upjohn Company, Kalamazoo, Michigan.

REFERENCES

Ashworth, M. A., and Haist, R. E. (1956). *Canad. med. Ass. J.*, **74**, 975.
Bell, D. M. (1952). *J. Lab. clin. Med.*, **40**, 337.
Berson, S. A., Yalow, R. S., Bauman, A., Rothschild, M. A., and Newerly, K. (1956). *J. clin. Invest.*, **35**, 170.
Bolinger, R. E., and Grady, H. J. (1957). *Amer. J. med. Sci.*, **233**, 182.
Butterfield, W. J. H., Camp, J. L., Hardwick, C., and Holling, H. E. (1957). *Lancet*, **1**, 753.
Cahill, G. F., jun., Hastings, A. B., and Ashmore, J. (1957). *Diabetes*, **6**, 26.
Colwell, A. R., jun., Colwell, J. A., and Colwell, A. R., sen. (1956). *Metabolism*, **5**, 749.
Cox, R. W., Henley, E. D., and Williams, R. H. (1956). *Diabetes*, **5**, 366.
Elrick, H., Hlad, C. J., jun., and Witten, T. (1955). *J. clin. Invest.*, **34**, 1830.
Foster, G. L. (1923). *J. biol. Chem.*, **55**, 291.
Friedenson, M., Rosenbaum, M. K., Thalheimer, E. J., and Peters, J. P. (1928). Ibid., **80**, 269.
Gey, G. O., and Gey, M. K. (1936). *Amer. J. Cancer*, **27**, 45.
Goetz, F. C., Gilbertsen, A. S., and Josephson, V. (1956). *Metabolism*, **5**, 788.
Holt, C. von, Holt, L. von Kracht, J., Kröner, B., and Kühnau, J. (1957). *Science*, **125**, 735.
Houssay, B. A., and Penhos, J. C. (1956). *Metabolism*, **5**, 727.
Lazarus, S. S., and Volk, B. W. (1957). Data presented at 39th Annual Meeting of Endocrine Society in New York City on June 1, 1957.
Loubatières, A. (1946). *Arch. Int. Physiol.*, **54**, 174.
Mirsky, I. A., Perisutti, G., and Diengott, D. (1956). *Metabolism*, **5**, 156.
Ogryzlo, M. A., and Harrison, J. (1956). *Canad. med. Ass. J.*, **74**, 977.
Purnell, R., Arai, Y., Pratt, E., Hlad, C., jun., and Elrick, H. (1956). *Metabolism*, **5**, 778.
Randle, P. J. (1956). *J. Endocr.*, **14**, 82.
Roe, J. H. (1955). *J. biol. Chem.*, **212**, 335.
Root, M. A. (1957). *Diabetes*, **6**, 12.
Scott, G. W., Prout, T. E., Weaver, J. A., and Asper, S. P., jun. (1957). Data presented at 17th Annual Meeting of the American Diabetes Association in New York City on June 1, 1957. To be published in *Diabetes*.
Somogyi, M. (1948). *J. biol. Chem.*, **174**, 189.
Teller, J. P. (1956). *Abstr. Pap. Amer. chem. Soc.*, 130th Meeting, 69c.
Vaughan, M. (1956). *Science*, **123**, 885.
Willebrands, A. F., and Groen, J. (1956). *Diabetes*, **5**, 378.
Williams, R. H., and Henley, E. D. (1957). *A.M.A. Arch. intern. Med.*, **99**, 501.
Wrenshall, G. A., and Hamilton, J. D. (1957). *Ann. N.Y. Acad. Sci.*, **71**, 154.
Zierler, K. L., and Andres, R. (1956). *J. clin. Invest.*, **35**, 991.

# INFERTILITY: ITS INCIDENCE AND HOPE OF CURE

BY

**HUBERT CAMPBELL, B.A., F.S.S.**

*5th-Year Student, Medical School, University of Durham*

The grief of a woman who has failed to bear a live-born child is a grief that has been known to the human race almost from its beginning. The first mention we have in ancient literature of a woman grieving over her infertility is of Sarai in Genesis xvi and xvii. There are three features of her case that are of interest even to-day. First, the infertility was of long duration, and had not responded to treatment. Secondly, it gave rise to marital disharmony: Sarai was convinced that she was the cause of her childlessness only after Abram had produced a child by her servant Hagar. Then, of course, her jealousy of Hagar and the child knew no bounds. Thirdly, when the child was ultimately born he was Isaac, the progenitor of the whole Jewish nation, and probably one of the most important men who ever lived.

These three points—the failure of therapy, the marital disharmony, and the great importance of the child who finally does arrive—are just as true to-day as they were four thousand years ago.

This illustrates that with infertility one is dealing with the whole of the religious, social, and economic, as well as the physiological and psychological, factors that influence human relationships. It emphasizes also that one is dealing not with a single patient but with a family. In consequence, it would be presumptuous if any author felt that he could write an article on such a subject in a purely detached manner, uninfluenced by his own moral judgments. But in so far as the rest of this paper is statistical I hope I have managed to maintain as objective a view as possible.

The purpose of this paper is to find (1) the extent of the problem of infertility, and (2) whether a woman who has failed to conceive after a short period of infertile marriage has a reasonable statistical chance of a future pregnancy. It is my conclusion that many who suffer short periods of infertility have a good chance of conceiving a child even after four to five years of infertile marital relations.

*Difficulty of Defining Infertility.*—The essence of the problem was put by Matthews Duncan (1866), the Edinburgh physician, nearly a century ago: "A reputation for curing sterility is spoken of as if it were founded on substantial claims. As in other departments of therapeutics there has been a great failure of logic, the *post hoc* and the *propter hoc* have been confused, a coincidence has been regarded as a consequence. . . ." The only criterion of infertility available is one of fact that a couple have not conceived, and this must not be confused with sterility—that a couple cannot conceive.

### 1951 Census of Great Britain

For a study of the whole country census data is available, but, although these data are tabulated according to the age of the wife, it should not be forgotten that it is a childless couple that is concerned in the problems of infertility.

All married women under the age of 50 at the date of the 1951 census were asked to give details of all the live-born children they had had, and also the date of their marriage. Those who had not borne a live-born child after 15 years of marriage are now considered to be cases of prolonged primary infertility.

The full report of the census has not yet been published, but a 1% sample was published in 1952 for the whole of Great Britain, and a 20% sample for Scotland was published in 1956.

The census reports enable us to establish how many women have never had a live-born child (Table I). It is thus apparent that there is a considerable degree of infertility existing in this country. The commonest age for a woman to marry is between 20 and 25, and even in this group 10% of couples are still infertile 15 years after marriage. The group who were married before they were 20 constitute a special case, as McKeown (1955) estimates that 73% of those who in 1939 were married under the age of 20 had already proved their fertility before marriage.

TABLE I.—*Married Women Not Having Borne a Live-born Child. Duration of Marriage* 15 *Years or Over Per* 100 *Total Married Women*

| Region | Age at Marriage | | | | | All Ages |
|---|---|---|---|---|---|---|
| | Under 20 | 20–24 | 25–29 | 30–34 | 35–* | |
| England and Wales | 4 | 10 | 20 | 34 | 51 | 12 |
| Scotland | 3 | 6 | 13 | 26 | 51 | 8 |
| Northern England | 2 | 8 | 15 | 35 | 56 | 9 |
| London and S.E. | 5 | 11 | 24 | 36 | 63 | 14 |

* Duration of marriage 10 years or over.

These results have been analysed in greater detail elsewhere (Campbell, 1957) where it is found that there is no significant difference in the extent of infertility between the various social or economic classes. It also appears that there is very little difference due to density of population but that there is less infertility in the north of the kingdom. Only wives of clerical workers and shop-workers are significantly more infertile at all ages.

It is not possible to take these figures at their face value without considering the effect of family limitation upon them.

### Data on Contraception

There can be no completely reliable data on contraceptive practices, as clinical samples are bound to be

unrepresentative and representative samples cannot be relied upon to give the whole truth.

Lewis-Faning (1949, Table 62) found that in a group of 3,281 women who were first interviewed in hospital in circumstances not connected with maternity, only 16.6% had endeavoured to postpone conception for more than six months after their marriage, and that 20% of these were unsuccessful in doing so. Only 2% had tried to postpone their first baby by more than five years. It would appear, therefore, that the effect of contraception on prolonged primary infertility must be slight; only this 2% who continued to practise contraception for more than five years could be truly described as voluntarily infertile.

Later in marriage 54% of these 3,281 women did use contraceptive methods; obviously in most cases this was after they had already proved their fertility and wished to restrict it.

Of the 99 women over 45 who had had no child, only four said that they were content to remain childless, and only 1% of the mothers of single children would have preferred not to have had more.

### Additional Data

There are additional data to suggest that the incidence of prolonged primary infertility was high in previous years. In 1911 11% of marriages had had no live-born child after 15 years. In 1855 in Edinburgh and Glasgow, Matthews Duncan found 15% of marriages sterile. He also quotes *Burke's Peerage* between 1833 and 1842 to show that 16% of the marriages amongst peers in the early nineteenth century were infertile.

It may be concluded, therefore, that in Great Britain 12% of all marriages, or one in eight, will remain infertile for at least 15 years, and that almost all of this infertility of prolonged duration is involuntary.

### When is Infertility a Legitimate Complaint?

If a woman has failed to give birth to a live-born child after 15 years of marriage, it is apparent that even if she has not reached the menopause she is very unlikely to succeed at all. But the time is then too late for her to seek a remedy either by medical treatment or by adoption. Consequently the question arises, "When should she start to worry about the problem?"

Matthews Duncan (1866) suggested after two years of marriage; to-day this has been interpreted as two years of normal intercourse, and it is still the general criterion in use. Bender (1952), however, pleaded for a shorter period of one year, as he calculated that 77% of the primigravidae admitted to the obstetrical units of the University of Liverpool had already conceived within 12 months. He quotes other hospital and special groups to show that the percentage of women who do conceive within a year is very high (Diddle, Jack, and Pearse, 1947, 86%; Scott Russell, 1946, 85%; Tietze *et al.*, 1950, 90%).

The census returns, however, do not support these findings that 80% of first conceptions take place within 12 months of marriage. In the 1% sample tables of the census there is not a table of primigravidae, but there are tables of the number of women remaining infertile after a given number of years of marriage (Table II).

So the number of married women who may justifiably complain of infertility is certainly greater than the one in eight who had no pregnancy after 15 years, and may be as great as the one in three who were not pregnant at the end of two years of married life.

TABLE II.—*Great Britain. Women Remaining Infertile After a Completed Number of Years of Marriage*

| Completed Years of Marriage | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 0-1 | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-10 | 10-15 | 15-25 |
| 86% | 55% | 38% | 30% | 25% | 20% | 18% | 16% | 14% | 13% |

But it is at this stage that we are pitched into the whole problem of contraception and voluntary postponement of the first baby. I know of no better estimates relevant to the period preceding the 1951 census than those of Lewis-Faning, quoted above, which indicate that, though it was common to limit a family after some children had been borne, it was not common to use birth control in the early stages of marriage, except amongst certain groups. Lewis-Faning's figures suggested that only 2% of couples postponed the first conception voluntarily for more than five years; the census figures show that 20% of the women with five years of marriage were still childless, but only 13% after 15 years. Hence some 7% of women first conceived between the 5th and 15th years of marriage.

Bender may be fully justified in accepting his criterion of 12 months of uncontracepted married life as a ground for complaints of infertility. I am merely trying to show that if Charles II was an unconscionable time a-dying, some babies are an unconscionable time arriving.

### What are the Chances of Pregnancy?

What are a woman's chances of a successful first pregnancy (*a*) in the coming year, or (*b*) before she is too old. Table III divides the women into the ages at which they were married and then traces the percentage of them remaining infertile through the years that followed. The data in this table are shown graphically in Fig. 1.

TABLE III.—*Great Britain. Married Infertile Women Per 100 Total Married Women*

| Duration of Marriage, Completed Years | Age at Marriage | | | | | Mean Duration of Marriage |
|---|---|---|---|---|---|---|
| | Under 20 | 20-24 | 25-29 | 30-34 | 35- | |
| 0-1 | 75 | 89 | 88 | 88 | 88 | ½ year |
| 1-2 | 36 | 55 | 59 | 60 | 75 | 1½ years |
| 2-3 | 22 | 39 | 39 | 45 | 64 | 2½ ,, |
| 3-4 | 17 | 28 | 30 | 37 | 63 | 3½ ,, |
| 4-5 | 14 | 22 | 27 | 33 | 62 | 4½ ,, |
| 5-7 | 11 | 14 | 21 | 31 | 56 | 6 ,, |
| 7-10 | 8 | 13 | 18 | 29 | 57 | 8½ ,, |
| 10-15 | 6 | 10 | 18 | 32 | 51 | 12½ ,, |

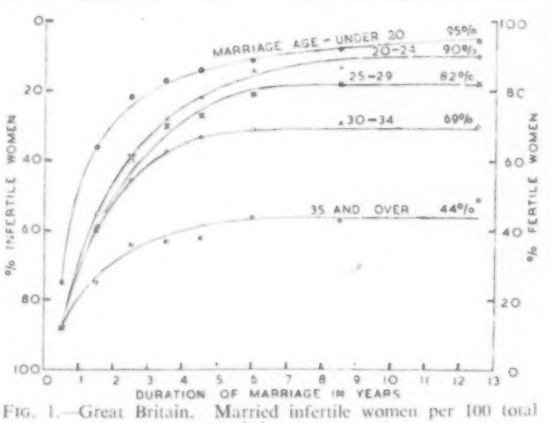



FIG. 1.—Great Britain. Married infertile women per 100 total married women.

Several important points emerge from this Table III and Fig. 1. Women who marry under 20 are distinctly more fertile than the rest, and those who marry over 35 are also markedly infertile, but between the ages of 20 and 34 there is very little difference in the earlier years of marriage. It should also be noted that 80% of women are married between these ages of 20 to 34, so I am not being unduly restrictive when proceeding to discuss these age groups in further detail.

If a hundred women between the ages of 20 and 24 were married in one year between January and December 31, then Table III states that on December 31 89 of them will not have had a baby and 11 will; therefore 11% will have a first live-born child in the first calendar year. (Note:

this is not the number who will have borne a child at the end of 12 months of marriage.)

There will be 89 women entering the second calendar year childless, of whom only 55 will remain so at the end of the year; thus we may conclude that 34 will have their first child in the second calendar year—that is, 38% of those entering it childless. In the third year 55 will enter it childless, but 16 will have a first child in that year—that is 29%—and so on. This is an actuarial technique similar to that used in an insurance life table, and is subject to the same limitations.

Migration and early death would affect the results if the incidence fell differently upon those with children and those without. There is some evidence that this is so, but the effect cannot be great.

As the first year is a special case, and the patients are unlikely to complain of infertility in the first year of marriage, this year has been omitted.

Table IV cannot be regarded as accurate in every detail, but the overall picture which it portrays may be taken as correct. It indicates that a woman who married between the ages of 20 and 24 has even after five years of infertile marriage, a 24% chance of giving birth *within the next 12 months*. These are odds of 3 to 1, which cannot be considered long odds.

TABLE IV.—*Great Britain. Chances of a Child in the Ensuing Year. Married Women Bearing a First Child During Each Year of Marriage as a Percentage of Those Who Started That Year as Infertile*

| Duration of Marriage | | Age at Marriage | | |
|---|---|---|---|---|
| Completed Years | Average Duration | 20–24 | 25–29 | 30–34 |
| 1–2 | 1½ years | 38 | 33 | 32 |
| 2–3 | 2½ ,, | 29 | 32 | 25 |
| 3–4 | 3½ ,, | 28 | 25 | 18 |
| 4–5 | 4½ ,, | 25 | 16 | 11 |
| 5–6 | 5½ ,, | 24 | 13 | 6 |
| 6–7 | 6½ ,, | 19 | 9 | 3 |

### Chances of Ultimate Success

Is it possible to offer some estimate of the probability that a woman may conceive before she is too old? From Table III and Fig. 1 it is clear that approximately 10% of all women married between the ages of 20 and 24 will remain childless, so of 100 women married in any one year 90 will ultimately have a child. Of the 89 who enter the second calendar year of marriage without a child, 79 will ultimately succeed—that is, 89%; of the 55 who enter the third year 82%; of the 39 who enter the fourth year 74%, etc. Table V indicates what percentage of women who have had a given number of years of infertile marriage will have a live-born child before they are too old to do so.

TABLE V.—*Great Britain*, 1951. *Chances of Ultimate Fertility. Percentage of Married Infertile Women Who Will Ultimately be Fertile*

| Duration of Infertile Marriage | Age at Marriage | | | Average Duration of Infertile Marriage |
|---|---|---|---|---|
| | 20–24 | 25–29 | 30–34 | |
| At marriage .. | 90 | 82 | 69 | Nil |
| 0–1 years .. | 89 | 80 | 65 | 6 months |
| 1–2 years .. | 82 | 69 | 48 | 1½ years |
| 2–3 .. .. | 74 | 54 | 31 | 2½ ,, |
| 3–4 .. .. | 64 | 40 | 16 | 3½ ,, |
| 4–5 .. .. | 55 | 33 | 6 | 4½ ,, |
| 5–6 .. .. | 43 | 17 | 3 | 5½ ,, |

Let us examine the example in Table V which we examined in Table IV. A woman who married between the ages of 20 and 24 and was still childless after five years has a 43% chance of having a child ultimately. These odds are of 6 to 4.

There is a considerable difference between the women married in their early thirties and those married in their early twenties. Table IV shows that for a few years they started as briskly as the younger ones, but Table V shows that their ultimate chances of success are very much less. They are good starters but poor runners.

### Additional Data

At the census every woman who had borne a live-born child during the 12 months preceding the night of the census was separately enumerated; thus it has been possible to estimate, from the actual records of live-born children, which women had terminated a period of primary infertility in the year before the census; the method is described in detail in a previous paper (Barns, Campbell, and Snaith, 1953). This method suggested that 12% of infertile married women had a first live-born child in the sixth year of marriage. This may be compared with the estimate of 13% at ages 25–29 in Table IV.

*Clinical Data.*—Barns *et al.* (1953) also examined 1,208 patients who attended the infertility clinic at the Newcastle General Hospital complaining of primary infertility. It was possible to follow 567 of them for at least two years, and there was no significant difference in pregnancy rates between those who had received some form of treatment and those who had not. These rates corresponded closely to those derived from the 1% sample of the census of Great Britain. These women were all trying to have a baby, and yet, making allowance for the duration of their infertility, fertility rates similar to those of the population at large were achieved. If the general population can achieve results as good as the clinic it does seem probable that the amount of *effective voluntary* infertility before the first child is born is not large. For birth control to be effective very careful attention to detail on every occasion is essential. Perseverance and care are not qualities widely distributed amongst the human race.

*1911 Census of England and Wales.*—At the 1911 census all married women were asked what number of children they had had, and how many were still alive. With this information it is possible to construct a table for the 1911 data similar to Table III. The general pattern is not dissimilar both with regard to the incidence of infertility and its remission. To take one example: of 100 women married between the ages of 20 and 24, 15 remained childless after an average of 3½ years; only 6 were to remain ultimately childless, thus 9 of them were to have a child after at least 3½ years of infertile marriage—that is, 60%. This compares with 64% of women in this age group and with this duration of infertile marriage in the 1951 census. It may be assumed that the incidence of appliance methods of contraception in 1911 was small, and hence less effective than to-day; consequently this 3½ years of infertile marriage was largely involuntary.

### Pathology

It is, of course, impossible to say anything about the extent of genital disease amongst the general population, but Bender (1952) and Barns *et al.* (1953) have something to say about the pathological conditions found in couples attending infertility clinics. Bender found that 15 out of 700 women were suffering from a tuberculous pelvis (2%), and Barns *et al.* found 11 out of 567, which is also 2%. Neither of them mentioned congenital anomalies of the genital tract, but presumably such cases would not be found amongst the voluntary patients at an infertility clinic.

Barns *et al.* state that they found one patient who had had a hysterectomy; 64 patients with tubal blockade, of whom 6 conceived; and 16 with other gross pelvic conditions, of whom 4 conceived.

Azoospermia was found by Bender in 39 out of 700 couples (6%) and by Barns *et al.* in 37 out of 567 couples (7%). This agrees with the findings of other workers: Davidson (1949) found 8% and Page and Houlding (1951) found 7%. If it is accepted that in 6% of couples the husband may be unable to produce adequate semen, then this would in itself explain Swyer's (1953) assertion that half of all infertility cases are due to failure of the male factor. But we must remember that these samples are doubly biased—first, because the wife voluntarily sought the assistance of the clinic,

and, secondly, because the husband consented to seminal analysis. A diagnosis of azoospermia may only make matters worse by allocating "blame" and by removing the one consolation a couple have—namely, hope; and unless it clears the way for adoption such a diagnosis may only increase marital disharmony.

The general conclusion is that pathological conditions are far outnumbered by functional disorders and by infrequent coitus.

### Treatment

There have been several papers on the subject of treatment in the last few years. It is worth while consulting Bender (1952), Barns *et al.* (1953), and also Sharman (1952) and Gordon (1956). Gordon gives an excellent review of the whole situation. The general conclusion is rather negative: "The value of the infertility clinic for therapeutic purposes appears to be slight" (Barns *et al.*, 1953). "What is needed is the realization that there is an optimum time to stop all investigations and all treatment before they become obsessed with their failure" (Gordon, 1956).

### Other Literature

Raymond Pearl (1939) selected a group of 199 women from Baltimore who stated that they had never practised any form of birth control, and who had had at least one child; he followed them for 12 years on average, and obtained a record of their coital history. The average monthly frequency was 10.5. If only potentially effective copulations be considered—that is, omitting those that took place when the wife was already pregnant or during puerperium—then there were 254 of these for every pregnancy, and 301 for each live birth. So the average time taken to conceive was roughly 24 months. He concludes: "The relative sterility of the human organism is truly the marvel rather than its fertility."

Scott Russell (1946) analysed a group which included 197 primiparae who were attending the Radcliffe Infirmary, Oxford, during the latter years of the war. Nearly two-thirds of these pregnancies took place within three months of starting normal coitus; he also found that over 60% admitted, when cross-examined in detail, that they had used some method of birth control. Nearly two-thirds of these had used coitus interruptus.

He suggests that Pearl's group were using coitus interruptus but did not admit that it was a method of contraception. It seems unlikely that Pearl had overlooked this point or, having appreciated it, failed to elicit the correct answers, as 20% of his larger group of 31,000 had admitted using this method. Furthermore, coitus interruptus cannot be considered an effective method of contraception.

Another very interesting paper is that of Diddle *et al.* (1947). They were medical officers in charge of a U.S. Naval base which was situated on an island off the coast of Florida. Married quarters were provided, but the husbands were all liable to be posted to war theatres at short notice; they were allowed to sleep at home two nights out of three. Amongst the 1,192 married women included in the survey no contraceptive measures were used. Their average age was 24.

Of the primigravidae who became pregnant whilst at the base 86% had conceived within the first 12 months of trying for a baby. This figure agreed with those of Russell (85%) and was later to be confirmed by Bender (77%), Tietze *et al.* (90%), and others. Unfortunately it was interpreted as meaning that 86% of normal women should conceive within 12 months of starting natural intercourse. *It does not mean this at all.* In the words of Matthews Duncan 80 years previously, "the *post hoc* and the *propter hoc* have been confused." To obtain this figure 251 women who had not had a pregnancy at all had been excluded.

Fortunately Diddle *et al.* had a relatively closed community, so it was possible to deduce the rates at which these women were becoming pregnant. At the beginning of the survey 866 of them were nulliparous. 615 (71%) of these became pregnant before it was discontinued; 350 (41%) were pregnant within six months; 133 (15%) in between six and twelve months; 78 (9%) in one to two years; and 54 (6%) in over two years. 251 remained without child.

If we wish to compare these women with those in the U.K. Census an allowance must be made both for pregnancies which terminate before term and for stillbirths. It is only possible to do this roughly, and it has been arbitrarily assumed that 10% of clinically diagnosed pregnancies would fail to produce a live-born child. The Royal Commission on Population assumed 7–11% abortions and 2–3% stillbirths.

Nine months must also be added to the dates at which the pregnancies took place to arrive at the time the baby was born.

The results may be compared with those of Table II for women aged 20–24 enumerated in the U.K. Census of 1951, as these are of a similar age. These results are summarized in Table VI and plotted on Fig. 2.

TABLE VI.—*Percentage of Married Women Remaining Infertile*

| U.K. 1951 Census | | | U.S.N. Wives | | | |
|---|---|---|---|---|---|---|
| Months Married | Mean Duration | % | Months Married | Mean Duration | % Unadjusted | % Adjusted |
| 0–11 | 6 | 89 | 9–14 | 12 | 60 | 64 |
| 12–23 | 18 | 55 | 15–20 | 18 | 44 | 50 |
| 24–35 | 30 | 39 | 21–32 | 27 | 35 | 42 |
| 36–47 | 42 | 28 | 33– | 39 | 29 | 36 |
| 48–59 | 54 | 22 | | | | |

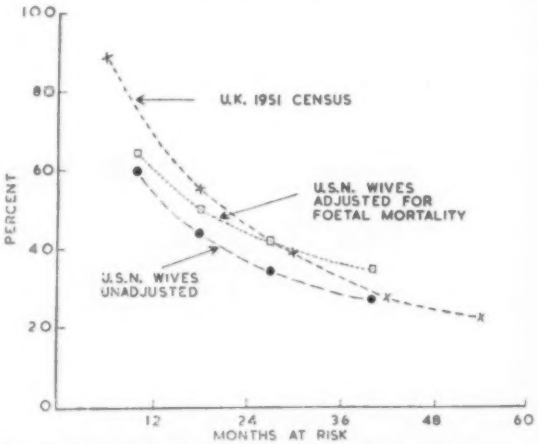



FIG. 2.—Percentage of women remaining infertile: U.K. census, 1951, compared with data of wives of United States naval personnel.

If the figures in Table VI and the graphs in Fig. 2 are compared it is surprising how similar are the two series—on the one hand the U.K. Census population, on the other the selected wives of U.S. Naval personnel. These American women were all married to fit, vigorous husbands; they were all willing to conceive; there was no contraception; the pathological cases had been excluded and the frequency of coitus was estimated at about 10 per month, yet the British women in the 1951 Census did very little worse than the American women. To me this seems a clear indication that in Great Britain the effect of contraception in postponing the birth of the first child is not very great.

So the figures of Diddle *et al.* show that 86% of those who conceived did so within one year, which is in full agreement with the other obstetricians' findings. But these figures also show that at least 44% of the women had failed to produce a live-born child at 18 months (if an allowance of 10% loss in the gestation period is allowed, then 50% would be without child at 18 months) compared with 55% of the British population.

Thus Diddle *et al.* agree with both sides in this argument between statisticians and the obstetricians, and the great and

careful detail of their paper enables us to see what is the difference between examining only those who succeeded and examining those who set up to try.

## Discussion

The first problem is to define what is meant by an infertile couple, and in the first part of this paper a very rigorous definition has been maintained—namely, 15 years of married life without a child. It is clear from experience and also from Lewis-Faning's questionary that very few of the women who are childless after 15 years are so of their own free will. Probably less than two in every hundred will admit that they are not disappointed to be without children. Yet even by this rigorous definition 12% of marriages in England and Wales which had endured for 15 years on the Census night had not had a single live-born child.

It is difficult to say how much of this infertility is due to failure in gestation rather than failure in conception. We know that the stillbirth rate in 1951 was about 2.3%, and that the Royal Commission on Population believed that between 7 and 11% of pregnancies terminated in abortion, but we do not know whether this is associated with ultimate childlessness.

When we come to consider a less rigorous definition of infertility it is impossible to draw a clear line anywhere between fertile and infertile, and consequently the only real answer to the problem has been to consider a group of women married at a given age and time, and see at what rate they do in fact produce their first babies.

These results must not be accepted uncritically as representing the physiological norm. It is obvious that the influence of family planning must be considered, but it is most difficult to obtain any quantitative estimates of the prevalence of contraception before the birth of the first child.

In general, Scott Russell, Lewis-Faning, and Pearl agree that in a modern community approximately 60% of married couples resort to contraception. But the effectiveness of this is a very different matter, and the stage of marital life at which it is practised is another. I believe that in fact contraception has only a small influence in postponing the first birth. The 1911 data show that even 45 years ago a considerable proportion of women remained infertile for several years, and yet proved their fertility after a lapse of time. There is little social or economic effect on the extent of the problem (Campbell, 1957).

The clinical data of Barns *et al.* show that a group of women who were attending a fertility clinic did very little better than the rest of the population. Diddle *et al.* show that a selected group of wives of American Service men follow the same trends of fertility as those of the Census figures.

All of these arguments have persuaded me that it is possible to accept the figures in Tables IV and V as portraying something resembling the truth—for instance, that a woman married between the ages of 20 and 24, and infertile for five years, has a fifty-fifty chance of a baby. It must be remembered, however, that the management of an individual case of infertility can never be an abstract problem in statistics. As was emphasized by Russell and Mitchell (1954), the doctor who is dealing with a case of infertility is treating not only a patient but also a marriage, and the criterion of his success is not only whether a pregnancy supervenes but also, and perhaps primarily, whether the couple learn to cope amicably with their problem. These tables offer hope to such a doctor, for if he feels in his own heart that there is a good chance of success there will be a ring of conviction in his advice to the couple to "go home and don't worry."

I know that by printing precise figures I suffer the risk of them being interpreted too precisely; but my intention is that these tables should be examined as a whole, and the conclusion I draw from them is that a woman who has suffered several years of infertile marriage still has excellent chances of conception if she perseveres in tranquillity and hope.


## Summary

The difficulty of defining an infertile marriage is discussed.

If prolonged primary infertility is defined as 15 years of marriage without a single live-born child, then the incidence in Great Britain in the 1951 Census was 12% of surviving marriages.

The effect of family limitation on this figure is considered. It is concluded that the effect is negligible.

A clinical definition of infertility is considered. Matthews Duncan suggests two years of marriage; Bender suggests 12 months of uncontracepted marital life.

It is shown that if these definitions are accepted there is a very high incidence of spontaneous remission.

Tables are calculated from the 1951 Census data to show, after a given number of years of infertile marriage, the probability of a pregnancy within the next 12 months and the probability of a pregnancy before the menopause.

The influence of family planning on these figures is considered. The extent of this influence cannot be accurately assessed, but reasons are offered to suggest that the influence of effective contraception on first births is not very great.

The figures are compared with those of other workers: (*a*) Newcastle General Hospital Fertility Clinic conceptions. (*b*) The frequency of live-born children to previously infertile women in the 12 months preceding the 1951 Census. (*c*) The results of the 1911 Census. (*d*) The findings of Raymond Pearl in the Eastern States of America. (*e*) The findings of Diddle, Jack, and Pearse amongst the wives of U.S. Naval personnel.

It is concluded that many women fail to conceive over a period of several years, although having normal marital intercourse; that their chances of an ultimate success, in the absence of overt pathology, remain good while under the age of 35, even without medical treatment; and consequently that a woman attending an infertility clinic who is without overt disease may be given every assurance to encourage her to continue to try to conceive.


I wish to acknowledge the assistance of Mr. Linton Snaith, who introduced me to the subject as a matter for study and has read and commented upon the paper, and to Mr. J. K. Russell, who has also made several helpful suggestions. I am also indebted to Mrs. Angley for the typing, to Mrs. Weightman for the graphs, to my wife for comments, and to my children for inspiration.

### REFERENCES


Barns, T., Campbell, H., and Snaith, L. (1953). *J. Obstet. Gynaec. Brit. Emp.*, **60**, 6 0.

Bender, S. (1952). *Brit. med. J.*, **2**, 409.

Campbell, H. (1957). *Univ. Durh. med. Gaz.*, **51**, 101.

Davidson, H. A. (1949). *Brit. med. J.*, **2**, 1328.

Diddle, A. W., Jack, R. W., and Pearse, R. L. (1947). *Amer. J. Obstet. Gynec.*, **54**, 57.

Duncan, J. Matthews (1866). *Fertility, Fecundity and Sterility*. Edinburgh.

General Register Office—Census of England, 1851, vol. I.

—— (1914). Census of 1911, Fertility, Pt. I.

—— (1953). One per cent Sample Tables, Pt. II, of Census 1951. Fertility of Marriages.

General Registry Office of Scotland—Census of Scotland, 1861, vol. II.

—— (1956). Twenty per cent sample of the 1951 Census. Fertility of Marriages in Scotland.

Gordon, D. W. S. (1956). *St. Mary's Hosp. Gaz.*, **61**, 124.

Lewis-Faning, E. (1949). *Family Limitation*. Papers of the Royal Commission on Population, vol. I. London.

McKeown, T. (1955). *Brit. med. J.*, **2**, 1325.

Page, E. W., and Holding, F. (1951). *Fertil. and Steril.*, **2**, 140.

Pearl, R. (1939). *Natural History of Population*. London.

Russell, C. S. (1946). *Lancet*, **1**, 300.

Russell, J. K., and Mitchell, A. P. B. (1954). Ibid., **1**, 1161.

Sharman, A. (1952). *J. Amer. med. Ass.*, **148**, 603.

Swyer, G. I. M. (1953). *Proc. roy. Soc. Med.*, **46**, 835.

Tietze, C., Guttmacher, A. F., and Rubin, S. (1950). *Fertil. and Steril.*, **1**, 338.

# ACUTE RENAL FAILURE ASSOCIATED WITH MASSIVE HAEMORRHAGE IN A HAEMOPHILIAC

BY

**D'ALMERO KOK, M.D., B.Sc., M.R.C.P.**
*Lecturer in Medicine, University of Cambridge*

AND

**P. BARKHAN, M.D., B.Sc.**
*Elmore Research Student, Department of Medicine, University of Cambridge*

Acute renal failure has recently been discussed by Milne (1957), and the clinical features have been described by Bull, Joekes, and Lowe (1955, 1956, 1957). One of the principal causes is renal ischaemia, which may result from acute renal circulatory insufficiency in conditions involving haemorrhage and shock. Acute renal failure might therefore be expected to occur in haemophiliacs after massive haemorrhage. This has not, to our knowledge, been recorded, although Macfarlane *et al.* (1957, Case 10) have described a case of acute tubular necrosis caused by hypotension occurring in a haemophiliac during a lengthy and extensive operation. This was performed under cover of parenterally administered beef antihaemophilic globulin (A.H.G.), and was not associated with much bleeding. The following case is therefore worth reporting.

## Case Record

A man aged 44 had suffered from repeated episodes of haemorrhage all his life. His elbow-, knee-, and ankle-joints were deformed, and showed radiological changes consistent with those due to haemophilia. A brother had died in infancy after circumcision.

On May 13, 1956, he developed a severe pain in the abdomen during a bout of coughing. A haematoma then appeared in the epigastrium. During the next few days the pain ceased and the blood started tracking downwards. On waking on May 19 the pain had returned, and he was unable to pass water. In the course of the day his abdomen became distended, the pain increased in intensity, and he started vomiting small quantities of altered blood. He managed to pass only a very small quantity of blood-stained urine. By the afternoon he was found to be in a state of shock, with a blood pressure of 90/60 and a pulse rate of 140 a minute, and was admitted to a local hospital. A blood transfusion was given that evening, after which his blood pressure rose to 130/98. He was then transferred to Addenbrooke's Hospital.

On admission his lower abdomen was discoloured, tense, and tender, and measured 44 in. (112 cm.) in circumference. His girth was normally about 38 in. (96.5 cm.). His blood pressure was 135/85 and pulse rate 140. Catheterization produced only 60 ml. of grossly blood-stained urine. He remained anuric for the rest of the day.

*Laboratory Findings.*—Haemoglobin, 10.8 g./100 ml.; leucocyte count, 6,700/c.mm.; platelets, 430,000/c.mm.; blood urea, 60 mg./100 ml. Thromboplastin generation test —method of Biggs and Douglas (1953) as modified by Bell and Alton (1954): A.H.G., 15% of normal activity. Christmas factor, normal activity.

The diagnosis of classical haemophilia (A) was therefore confirmed; the patient had obviously had a large haemorrhage into the abdominal wall, and it was thought that he had also developed acute renal failure. A prophylactic transfusion of fresh plasma and blood (1 litre of each) was given, fluids were restricted, and glucose (20%) and appropriate amounts of saline were administered intravenously.

He remained oliguric during his first two days in hospital, passing less than 75 ml. of urine in 24 hours. Diuresis started on the third day after admission. The urine was no longer blood-stained, but bleeding into his abdominal wall occurred again on the third and fourth days in hospital, the haematoma becoming more tense and painful, his girth increasing to 45 in. (114 cm.), and his haemoglobin level falling to 5.2 g./100 ml. A further transfusion of 2 litres of fresh blood was therefore given. His blood pressure did not fall below 120/80 at any time, and his diuresis was not interrupted, although his blood urea rose progressively to a level of 380 mg./100 ml. on the fifth day after admission. Thereafter his general condition improved, and his haematoma regressed. In view of the falling level of serum potassium noted at that time, he was given 8 g. of potassium citrate daily by mouth. After the 10th day in hospital the serum potassium level started to rise.

On the sixteenth day after admission it was noticed that his haemoglobin level had dropped to 7.3 g./100 ml. There were no accompanying symptoms or signs until the eighteenth day, when a large melaena stool was passed. Blood and plasma transfusions were started again, and 3 litres of plasma and 4.5 litres of blood were given over a period of three days. His blood pressure did not fall below 100/60 during this episode, and his urinary output was maintained satisfactorily. However, his blood urea rose from 130 to 170 mg./100 ml., and his serum potassium fell once more. At this stage it was thought necessary to treat him with potassium intravenously as well as by mouth. For the sake of convenience, potassium citrate was added to the blood which was being transfused at the time, the dose given amounting to 2.78 g./litre, or 25 mEq of potassium per litre. Whenever the rate of the transfusion with added potassium was increased above 50 drops a minute (3 ml. a minute) the patient developed a severe pain along the course of the vein into which the blood was running. When the rate of infusion was decreased the pain was relieved within a few minutes. Blood, plasma, or glucose–saline without added potassium did not on any occasion produce a similar pain.

After this incident the patient's recovery was uninterrupted. Forty days after admission his blood urea had fallen to 20 mg./100 ml.; the specific gravity of his urine varied between 1004 and 1016, and it contained no protein. On readmission four months later his urine was still protein-free, and its specific gravity varied between 1004 and 1028.

The urine volume, blood urea, haemoglobin, and serum electrolyte changes during his illness are recorded in the Chart.

## Discussion

The patient had been severely oliguric for 72 hours, and had undoubtedly developed acute renal failure, although absorption of blood from the haematoma and to some extent from the gut had contributed to the level of his blood urea. The pattern of change of the serum electrolytes, together with the progressive increase of blood urea during the oliguric phase of his illness and its continued rise after the onset of diuresis, suggests that the failure was due to acute tubular necrosis. This was most probably caused by hypotension resulting from the acute blood loss on the day before his admission to Addenbrooke's Hospital. This concept is supported by the absence of any marked exacerbation of renal failure during subsequent episodes of haemorrhage on the third and particularly the eighteenth day in hospital, when the patient's blood pressure had been adequately maintained by prompt transfusion.

Obstruction of the ureters by external pressure from the haematoma can be excluded as a cause of the uraemia, because further bleeding into the haematoma occurred on the third and fourth days in hospital without affecting the diuresis, which had then just started.

During the oliguric phase of his illness large volumes of plasma and blood were necessary to stop further bleeding and also to raise the haemoglobin level. In view of the necessity for fluid restriction and a high carbohydrate intake, a 20% solution of glucose was given intravenously for

several days, and it was interesting to note that venous thromboses did not occur at the sites of infusion.

Pain along the course of a vein into which potassium is being infused has been reported (Semler, 1925 ; Pudenz *et al.*, 1938 ; Nadler *et al.*, 1950). The majority of instances occurred after the use of concentrated solutions of potassium chloride (2–10%), given within a matter of minutes. A few were observed after a 1.14% solution of potassium chloride (155 mEq of potassium per litre) had been given at the rate of 3–5 ml. a minute. However, during the treatment of diabetic ketosis, once diuresis has started, solutions containing up to 30 mEq of potassium per litre are frequently given at a rate of 3 ml. a minute without causing pain. In our case pain was caused by an infusion containing practically the same concentration of potassium (25 mEq/l. as potassium citrate plus 5–7 mEq/l. in the plasma of the blood), given at the same rate, suggesting that a low threshold of excitability was present in the pain receptors in the vein wall.

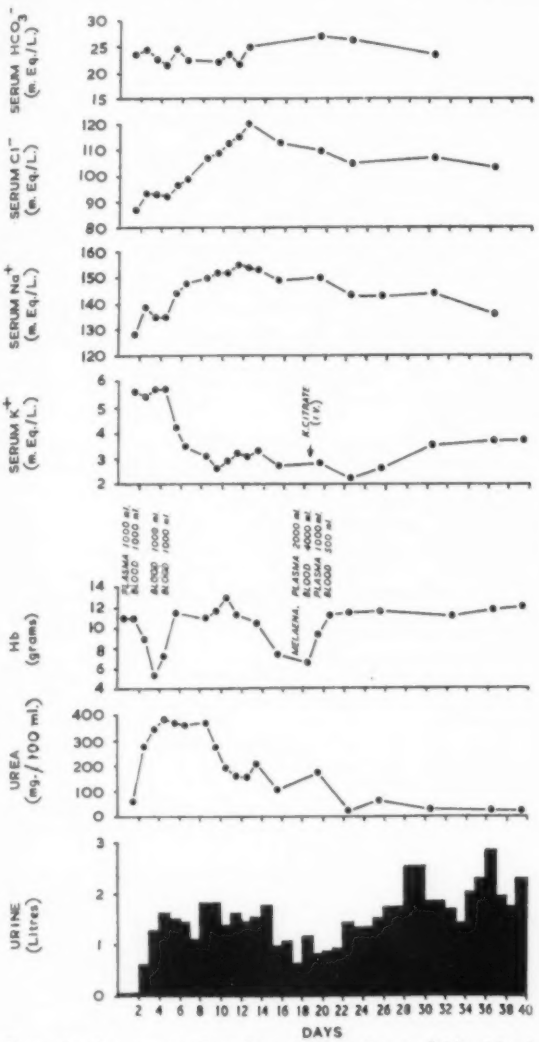



Chart showing serum electrolyte changes, haemoglobin, blood urea, and volume of urine during patient's stay in hospital.

It is known that spontaneous activity may be induced experimentally in nerve fibres by exposing them to potassium, which lowers the threshold of excitability (Brown and MacIntosh 1939). The same effect may be produced by sodium citrate, which removes ionized calcium and increases the ratio of potassium to calcium ions acting on the nerve fibre (Katz, 1936 ; Brink and Bronk, 1937 ; Lehmann, 1937). Presumably the non-medullated nerve fibrils which subserve pain respond in a similar manner.

In our case the blood being transfused contained 2 g. (1%) of disodium citrate as an anticoagulant, as well as 1.5 g. (0.278%) of added potassium citrate. It is probable, therefore, that the lowering of the pain threshold was due to potentiation of the potassium effect by the citrate.

## Summary

Acute renal failure, with complete recovery, is reported in a haemophiliac after massive haemorrhage into the abdominal wall.

Treatment included transfusion with large volumes of fresh plasma and blood.

Potassium citrate was given intravenously for a time, and was found to produce local pain when a threshold concentration was exceeded.

We wish to thank Dr. C. B. V. Walker, of the Regional Blood Transfusion Service, Cambridge, for his unfailing co-operation.

### REFERENCES

Bell, W. N., and Alton, H. G. (1954). *Nature (Lond.)*, **174**, 880.
Biggs, R., and Douglas, A. S. (1953). *J. clin. Path.*, **6**, 23.
Brink, F., and Bronk, D. W. (1937). *Proc. Soc. exp. Biol. (N.Y.)*, **37**, 94.
Brown, G. L., and MacIntosh, F. C. (1939). *J. Physiol. (Lond.)*, **96**, 10P.
Bull, G. M., Joekes, A. M., and Lowe, K. G. (1955). *Lancet*, **2**, 1152.
—— —— —— (1956). Ibid., **1**, 186.
—— —— —— (1957). Ibid., **2**, 114.
Katz, B. (1936). *J. Physiol. (Lond.)*, **88**, 239.
Lehmann, J. E. (1937). *Amer. J. Physiol.*, **118**, 613.
Macfarlane, R. G., *et al.* (1957). *Lancet*, **2**, 251.
Milne, M. D. (1957). *Proc. roy. Soc. Med.*, **50**, 493.
Nadler, C. S., Bellet, S., Gazes, P. C., and Steiger, W. A. (1950). *J. Lab. clin. Med.*, **35**, 842.
Pudenz, R. H., McIntosh, J. F., and McEachern, D. (1938). *J. Amer. med. Ass.*, **111**, 2253.
Semler, R. (1925). *Klin. Wschr.*, **4**, 697.

# SALT RETENTION AND URAEMIA IN BRAIN INJURY

BY

**R. J. S. METZ, M.B., B.Ch.**
*Medical Registrar*

AND

**W. COOPER, M.B., M.R.C.P.Ed.**
*Physician*

*Coronation Hospital and the University of the Witwatersrand, Johannesburg*

Cerebral disorders of various kinds may be followed by biochemical disturbance in which abnormally high levels of sodium and chloride in the blood are associated with extremely low levels of these ions in the urine. The term "salt-hoarding syndrome" has been suggested for this condition (de Wardener, 1956), and the term seems to be a satisfactory one so long as it is appreciated that uraemia appears to be an invariable concomitant of the hypernatraemia and hyperchloraemia.

This syndrome was first reported by Allott (1939), who observed it in association with cerebral haemorrhage, adenoma of the choroid plexus, and tuberous sclerosis. It has since been observed following a large variety of cerebral lesions. These include brain damage following head injuries (Higgins *et al.*, 1954), bulbar poliomyelitis (Allott, 1957), bilateral ligation of the anterior cerebral arteries (MacCarty and Cooper, 1951), operations on the pituitary (Cooper and MacCarty, 1951), leucotomy (McLardy, 1950), subarachnoid

haemorrhage, subdural haematoma, brain tumour, meningitis, Wernicke's encephalopathy, "encephalomalacia" (Schoolman *et al.*, 1955), right frontal lobectomy, removal of a glioma invading the third ventricle (Sweet *et al.*, 1948), and anoxia in premature infants (Natelson and Alexander, 1955). The picture of hypernatraemia, hyperchloraemia, and uraemia has also been seen in sulphonamide toxicity in which the drug caused both kidney and brain damage (Luetscher and Blackman, 1943; Goodale and Kinney, 1949).

The phenomenon of salt-hoarding associated with lesions of the brain is not a rare one: 63 such cases were seen in one hospital over a period of four years (Schoolman *et al.*, 1955), and others claim to have seen the condition frequently (Natelson and Alexander, 1955). Higgins *et al.* (1954) recently reviewed the findings in 76 consecutive patients with closed head injuries who had remained unconscious for more than twelve hours, and found that 12% developed hyperelectrolytaemia.

We report here a further case of this syndrome in a patient who had sustained a head injury. The case appears to have been a typical example of the salt-hoarding syndrome. The patient's blood volume was measured when there was marked hypernatraemia and hyperchloraemia. It is the first case of this kind, so far as we are aware, in which this investigation was performed. The result has a bearing on the problem of whether dehydration or "desiccation" plays an essential part in the production of the hyperelectrolytaemia.

## Case Report

An African man aged about 30 was transferred to Coronation Hospital on March 9, 1957, from a country hospital where he had been in a coma for three weeks. He had been found lying in the street, apparently having been assaulted. When seen by us he was semi-comatose, responding to painful stimuli. He was emaciated, weight 7 st. 3 lb. (45.8 kg.), height 5 ft. 6 in. (167.5 cm.). There were numerous large blebs filled with clear fluid distributed on the trunk and extremities. The tongue was somewhat dry, and clinically there appeared to be slight dehydration. The temperature was 97° F. (36.1° C.) the pulse rate was 120 a minute, and the blood pressure 90/60. The tendon reflexes appeared to be slightly brisker on the left, but otherwise there were no localizing neurological signs and all limbs were seen to be capable of movement.

The initial investigations showed the following results. Urine: specific gravity 1018, sugar and protein absent, microscopical examination showed no abnormality. Blood: leucocytes 13,000/c.mm., haemoglobin 13 g./100 ml. Electrocardiogram normal. Radiological examination of the chest showed no abnormality; radiological examination of the skull showed a linear fracture of the left parietal bone involving the base of the sphenoid. An air encephalogram showed nothing abnormal. Serological tests for syphilis were negative.

To combat the dehydration he was given 3 litres of fluid (1 litre of 5% dextrose in 0.9% sodium chloride, 1 litre of 0.9% sodium chloride, and 1 litre of 5% dextrose in water) intravenously in the first 15 hours. On the morning after admission blood analyses gave the following results: urea, 380 mg./100 ml.; chloride, 126 mEq/l.; sodium, 156 mEq/l.; potassium, 6.1 mEq/l.; $CO_2$, 13.5 mEq/l. The findings in the blood and urine relevant to the state of the patient's electrolytes are shown in Tables I and II. The blood urea was persistently elevated, rising still higher shortly before the patient's death on the tenth hospital day. The serum sodium and chloride, however, began to drop on the sixth day. There was no corresponding increase in the urinary levels of these electrolytes, which remained at extremely low levels throughout. The serum potassium, apart from a high initial level, remained within normal limits until two days before the patient's death, when the level fell below normal. There was no change in the urinary excretion of potassium, which remained scanty. It may be seen from the tables that in the first six days the picture was different from that in the last four days. In the first period there was hyperelectrolytaemia and good urinary output, whereas in the last few days there were normal levels of serum sodium and chloride, accompanied by oliguria.

TABLE I.—*Blood Urea (mg./100 ml.), Serum Electrolytes (mEq/l.), and Haematocrit*

| Date | Urea | Sodium | Chloride | Potassium | Bicarbonate | Haematocrit |
|---|---|---|---|---|---|---|
| March 10 | 380 | 156 | 126 | 6·1 | 13·5 | |
| ,, 11 | 372 | 165 | 133 | 4·7 | 18 | 43 % |
| ,, 12 | 360 | 165 | 141 | 4·4 | 16 | 43 % |
| ,, 13 | 328 | 162 | 134 | 4·2 | 21 | |
| ,, 14 | 332 | 156 | 131 | 4·2 | 15 | |
| ,, 15 | 345 | 151 | 113 | 4·6 | 15 | 41 % |
| ,, 16 | 400 | 141 | 120 | 4·0 | 16 | 42 % |
| ,, 17 | 444 | 139 | 108 | 5·4 | 16·8 | |
| ,, 18 | 536 | 148 | 107 | 3·6 | 18 | |
| ,, 19 | 492 | 142 | 103 | 4·1 | 18 | |

TABLE II.—*Urinary Findings: 24-hour Output (ml.); Specific Gravity; Urea (mg./100 ml.); Sodium, Chloride, Potassium (g./l.)*

| Date | Output | S.G. | Urea | Sodium | Chloride | Potassium | Remarks |
|---|---|---|---|---|---|---|---|
| March 10 | 1,600 | 1015 | | | | | |
| ,, 11 | 1,200 | 1015 | | | | | |
| ,, 12 | 1,700 | 1014 | | | | | |
| ,, 13 | 2,000 | 1014 | 2,080 | 0·68 | 1·62 | | |
| ,, 14 | 1,300 | 1015 | 1,680 | 0·74 | 1·63 | | |
| ,, 15 | 1,000 | 1012 | 1,920 | 0·63 | 0·382 | | |
| ,, 16 | 450 | 1012 | 1,220 | 0·88 | 0·32 | 0·15 | Urine contained pus |
| ,, 17 | 400 | 1012 | 1,160 | 0·96 | 0·275 | 0·15 | |
| ,, 18 | 500 | 1010 | 1,180 | 1·0 | 0·278 | 0·15 | |
| ,, 19 | 250 | 1012 | 980 | 1·4 | 0·32 | 0·14 | |

On the sixth day the blood volume was measured, using $^{51}Cr$ labelling of the patient's red cells. The total blood volume was 3,200 ml.—that is, 70 ml./kg. body weight—and the plasma volume calculated from the venous haematocrit was 2,100 ml. On the same day the plasma creatinine was 4.1 mg./100 ml. and endogenous creatinine clearance showed a value of only 11.4 ml. a minute. On the day before the patient's death the serum calcium was found to be 3.3 mEq/l., and the output of calcium in the urine was 35 mg.—that is, 14 mg./100 ml.

Throughout his stay the patient received fluids by vein or intragastric drip. Apart from the sodium chloride solution given on admission, and 2 litres of 6-molar lactate given on the sixth day to combat acidosis, these fluids were salt-free. The amount of fluid given daily was about 500 ml. in excess of the daily urinary output.

The patient's clinical condition deteriorated slowly. The systolic blood pressure remained at or just above 100 mm. of mercury. On the fourth hospital day a trace of protein appeared in the urine, and microscopical examination showed the presence of a few leucocytes and red cells, but no casts. It was thought that the indwelling catheter had caused a cystitis. Next day there was frank pyuria and haematuria and the patient became febrile. The urinary infection failed to respond to antibiotics. The patient died on the tenth hospital day.

### Necropsy Findings

Necropsy revealed slight organizing bruising in the left temporal muscle, a fine crack fracture in the left temporal region extending into the petrous temporal bone, slight haemorrhage into the sphenoidal sinus, marked generalized flattening of the cerebral convolutions, slight prominence of both unci, more marked on the right side. In the right temporal lobe on its lateral aspect were several areas of softening of the cortex over an area approximately 1½ by 1 in. (3.8 by 2.5 cm.). The surrounding brain substance

was very swollen and oedematous. There were occasional small areas of subarachnoid haemorrhage scattered over the brain surface. The pituitary fossa and pituitary gland showed no macroscopic evidence of damage. The lungs were congested and slightly oedematous and showed early signs of bronchopneumonia in both basal lobes.

*Kidneys.*—These appeared somewhat pale. The cut surface showed both the cortex and the medulla to be paler than normal. Microscopy showed some scattered areas of interstitial oedema. Dilatation of several tubules was seen, affecting mainly the distal tubules. There were scattered areas of interstitial infiltration with chronic inflammatory cells, and one or two areas of peri-glomerular fibrosis. An occasional vessel showed mild arteriosclerotic changes. There were a few pale hyaline casts. All the histological changes were of a minor degree.

*Other Findings.*—The bladder mucosa was very haemorrhagic. The lungs showed early changes of bronchopneumonia in both bases. The suprarenals were macroscopically normal.

## Discussion

It is generally agreed that in this type of case the brain damage is causally related to the metabolic changes. There has been no general agreement, however, on the possible mechanism of the biochemical derangement.

### Kidney

The role of the kidney itself has received scant attention. In none of the published cases was renal function thoroughly studied, yet in all those cases which we have traced in the literature the blood urea, where reported, was raised and usually markedly so. Schoolman *et al.* (1955) acknowledged the possibility of primary renal disturbance, but suggested that this disturbance could be the diuretic phase of "lower nephron nephrosis." They stated that in two of their cases of hypernatraemia "lower nephron nephrosis" existed. However, Allott (1957) has pointed out that the urinary findings in "lower nephron nephrosis"—namely, a low specific gravity, usually a high concentration of electrolytes, and a low concentration of urea—are in complete contrast with the findings in the salt-hoarding syndrome. Higgins *et al.* (1954) considered that the uraemia which may follow brain injury is of renal origin despite the absence of morphological changes in the kidney at necropsy. They have pointed out that the proteinuria and renal glycosuria which may follow cerebral injury afford evidence of renal dysfunction secondary to brain damage. Allott (1957) has noted an inverse relationship between creatinine clearance and hyperelectrolytaemia, and in our case the creatinine clearance was only 11.4 ml. a minute.

In most of the reported cases which have come to necropsy the kidneys were normal on histological examination, although some showed slight changes similar to those in the present case. It is not possible to state the significance of the changes seen in the kidneys of our patient. Even in acute renal disease with severe functional derangement, histological changes may appear to be almost negligible (Brun and Munck, 1957). That the kidney may in fact be damaged secondarily to brain dysfunction is suggested by the work of Cort (1947), who elicited renal cortical ischaemia and complete anuria following stimulation of the posterior orbital surface (area 13) in the cat. Higgins *et al.* (1954) reported that a constant finding in the brains of their cases with hypernatraemia and hyperchloraemia was damage to the undersurface of the frontal lobes, and McLardy (1950) placed the lesion necessary for the development of uraemia following leucotomy in area 47 in the orbital cortex. He advanced reasons for suggesting that in man this area may correspond to area 13 in the cat.

A critical evaluation of renal function in the salt-hoarding syndrome is obviously called for and might possibly provide a clue to the intermediate steps in the mechanism by which brain dysfunction could provoke renal dysfunction.

### Diabetes Insipidus

Following the work of Engstrom and Liebman (1953) several authors have suggested that the hyperelectrolytaemia following cerebral disease may be due to the development of acute diabetes insipidus in these cases. Engstrom and Liebman studied the effects of "pitressin" (vasopressin) and cortisone in a patient with anterior and posterior pituitary insufficiency. When pitressin was withheld the patient developed hyperchloraemia with low levels of sodium and chloride in the urine. The effect was exaggerated when pitressin was withheld and cortisone administered. Two patients in whom salt-retention had appeared following the removal of a craniopharyngioma had earlier been described by Peters (1948) and Welt *et al.* (1952) respectively. The mechanism was thought to be acute diabetes insipidus leading to extreme dehydration in patients who were too mentally confused to take fluids. Allott (1957) has suggested the following course of events in the salt-hoarding syndrome: an appropriately located injury to the brain leads to acute diabetes insipidus resulting in the flushing out of excessive amounts of electrolytes; this in turn stimulates the secretion of aldosterone, which is responsible for the salt-retention. In Allott's case the excretion of aldosterone on the day it was measured was 4.5 μg., the upper limit of normal in the particular laboratory being 2 μg. daily.

Others have suggested that the course of events is similar to that which existed in the case of Peters (1948)—that is, diabetes insipidus leading to severe dehydration in unconscious patients. There are, however, certain objections to these hypotheses. In the patient studied by Engstrom and Liebman (1953) the specific gravity of the urine did not rise above 1007, and in the patient of Welt *et al.* (1952) with the craniopharyngioma the specific gravity of the urine was 1005. In our case the specific gravity of the urine was 1018 on admission. Anthonisen *et al.* (1954) reported a typical case of this condition in which the urinary specific gravity was 1022, and Sweet *et al.* (1948) found the specific gravity to be 1030 in a case of hyperelectrolytaemia. In a case of Welt *et al.* (1952) the specific gravity of the urine was 1022 at the time when the serum chloride was markedly elevated. They considered that this makes diabetes insipidus quite unlikely. The other objection, which is related to the question of dehydration in these patients, is discussed below.

It is of interest that Engstrom and Liebman (1953) and Welt *et al.* (1952), whose work forms part of the basis for the hypothesis of diabetes insipidus in these cases, considered that the mechanisms of hyperelectrolytaemia following on intracranial lesions may differ with different intracranial lesions. The former two authors, while stating that there is no direct evidence to support the suggestion, thought that direct central-nervous control of renal function is possible.

We also feel that, although salt-hoarding may undoubtedly occur in diabetes insipidus, this mechanism does not operate in the type of case under discussion.

### Dehydration

It is most unlikely that simple dehydration could account for the phenomenon of intense salt conservation, especially in the presence of a normal or high urinary output. Some authors have postulated a more complex type of dehydration. Anthonisen *et al.* (1954) suggested that derangement of the "osmoregulatory centre" causes dehydration and that this in turn stimulates the "volume receptor" to initiate mechanisms responsible for salt retention. A similar disturbance of cerebral mechanisms controlling electrolyte and water balance was postulated by Cooper and MacCarty (1951), although their patient was not clinically dehydrated.

There have been a number of conflicting views on whether or not dehydration, from whatever cause, is an essential part of the mechanisms responsible for salt hoarding and uraemia. It has been suggested that in these cases as much as 40–50% of body water may be lost (Schoolman *et al.*, 1955), while others have stressed that their patients were not clinically dehydrated. In our patient the daily excretion of between

1 and 2 litres of urine with a specific gravity of 1012–1018 during the period of hyperelectrolytaemia, did not suggest dehydration. Study of the blood volume showed 70 ml. of blood per kg. of body weight. This figure would appear to exclude severe dehydration.

### Other Features

Two other features deserve mention. In the present case, as in other cases, the electrolytes in the blood returned to normal levels, although the urinary content of sodium chloride remained very low. This observation suggests that in addition to salt retention there is an internal shift of electrolytes in this condition. Allott (1957) also inferred that a redistribution within the body is the likely explanation.

The other point worthy of note in our case was the presence of numerous bullae on the body surface. McLardy (1950) considered these bullae to be evidence of a trophic change consequent on cerebral damage. Our patient thus exhibited two distinct manifestations of his brain injury—the trophic lesions and the biochemical changes. In none of McLardy's cases did the lesions appear within two months of the brain injury. In only one case did both uraemia and the trophic changes coexist, and this was in a patient with bilateral involvement of the orbital cortex.

### Conclusion

In attempting to discover a mechanism responsible for hyperelectrolytaemia provoked by cerebral dysfunction, it would seem advisable to bear in mind Selkurt's (1954) warning that "in view of the multiplicity of factors concerned with water and electrolyte balance that may be disturbed under the above circumstances, attempts to draw discrete conclusions from clinical observations are extremely hazardous." However, this type of case is not rare, and a planned approach, directed particularly at elucidating renal function, should result in progress in the understanding of this most interesting problem.

### Summary

A case of hyperelectrolytaemia following a brain injury is described. Uraemia appears to be an integral part of the biochemical upset.

Evidence is produced that severe dehydration is not responsible for this disturbance, nor is diabetes insipidus thought to be a likely causative factor.

It is pointed out that renal function has not been sufficiently studied to enable an assessment to be made of the role of the kidneys in the syndrome.

We wish to thank Dr. M. E. L. Tonkin, superintendent of Coronation Hospital, for permission to publish this case report; Dr. J. Kaufman, pathologist, South African Institute for Medical Research, for the pathological reports; and Dr. J. Metz for the blood-volume estimation. We are indebted to Miss J. M. M. Horn for the daily biochemical investigations.

REFERENCES

Allott, E. N. (1939). *Lancet*, **1**, 1035.
—— (1957). Ibid., **1**, 246.
Anthonisen, P., Hilden, T., and Thomsen, A. C. (1954). *Acta med. scand.*, **150**, 355.
Brun, C., and Munck, O. (1957). *Lancet*, **1**, 603.
Cooper, I. S., and MacCarty, C. S. (1951). *Proc. Mayo Clin.*, **26**, 354.
Cort, J. H. (1947). Quoted by R. B. Livingstone *et al.*, *Ass. Res. nerv. Dis. Proc.*, 1948, **27**, 405.
de Wardener, H. E. (1956). In *Progress in Clinical Medicine*, 3rd ed., edited by R. Daley and H. Miller. Churchill, London.
Engstrom, W. W., and Liebman, A. (1953). *Amer. J. Med.*, **15**, 180.
Goodale, W. T., and Kinney, T. D. (1949). *Ann. intern. Med.*, **31**, 1118.
Higgins, G., Lewin, W., O'Brien, J. R. P., and Taylor, W. H. (1954). *Lancet*, **1**, 61.
Luetscher, J. A., and Blackman, S. S. (1943). *Ann. Intern. Med.*, **18**, 741.
MacCarty, C. S., and Cooper, I. S. (1951). *Proc. Mayo Clin.*, **26**, 185.
McLardy, T. (1950). *J. Neurol. Neurosurg. Psychiat.*, **13**, 106.
Natelson, S., and Alexander, M. O. (1955). *A.M.A. Arch. Intern. Med.*, **96**, 172.
Peters, J. P. (1948). *New Engl. J. Med.*, **239**, 353.
Schoolman, H. M., Dubin, A., and Hoffman, W. S. (1955). *A.M.A. Arch. intern. Med.*, **95**, 15.
Selkurt, E. E. (1954). *Physiol. Rev.*, **34**, 287.
Sweet, W. H., Cotzias, G. C., Seed, J., and Yakovlev, P. (1948). *Ass. Res. nerv. Dis. Proc.*, **27**, 795.
Welt, L. G., Seldin, D. W., Nelson, W. P., German, W. J., and Peters, J. P. (1952). *A.M.A. Arch. intern. Med.*, **90**, 355.

# APPENDICITIS AND ACUTE TERMINAL ILEITIS DURING AN OUTBREAK OF GASTRO-ENTERITIS AMONG BRITISH TROOPS IN PORT SAID

BY

**D. J. COWAN, F.R.C.S.**
*Major, R.A.M.C.*

During the period of occupation of Port Said from November 5 to December 18, 1956, of the 919 British troops who were admitted to medical units 365 had acute gastro-enteritis. Of the 29 patients admitted with suspected acute appendicitis 14 were subjected to laparotomy: 10 of these had acute suppurative appendicitis and three had acute terminal ileitis. The operations were in every case performed by me. Clinical details of the cases of terminal ileitis are presented.

All patients were young men living under similar conditions, the majority in vacated buildings in Port Said. In view of the damage to water mains and sewage, tap-water was unsafe for drinking, and all water supplied to troops was sterilized, either in bulk or by individual sterilizing tablets (halazone). During the early weeks of the occupation tinned "compo" rations were consumed.

The incidence of gastro-enteritis was higher in units where living conditions and hygiene were below the general standard, flies being particularly prevalent in such areas. In ships anchored in the harbour, where there were few flies, gastro-enteritis was uncommon.

### Clinical Description

There appeared to be two different groups of patients with gastro-enteritis. *Group 1.*—A small group of patients presented with the typical picture of bacillary dysentery and had profuse diarrhoea with blood and mucus in the stools; most of these cases occurred in one unit in a forward position. *Group 2.*—The majority of cases occurred among troops stationed in Port Said itself. These presented with high sustained fever, frontal headache, and occasionally neck rigidity. This was followed by severe abdominal colic and profuse diarrhoea 12 to 24 hours later. Few of these cases had blood or mucus in their stools. Recovery usually occurred after four or five days' illness, and relapses were rare. Skin rashes were not observed, nor did rheumatic symptoms occur. Dengue and sandfly fever were excluded on clinical grounds.

*Treatment.*—All cases received sulphonamides in some form or other, so that it is impossible to predict whether they would have recovered equally quickly without treatment. It was the general impression, however, that sulphonamides had little effect on the course of the disease of the patients in group 2.

*Pathology.*—Unfortunately only very limited pathological facilities were available. No cultures or agglutination reactions could be performed. Bacillary cellular exudate was found in the stools of patients in group 1 only. Moderate leucocytosis was the rule, with a preponderance of neutrophil granulocytes. Blood slides taken to exclude malaria were consistently negative.

### Incidence of Appendicitis

About one-third of the patients in group 2 had right-sided abdominal pain and tenderness, simulating appendicular pain, at some time during the course of their illness. Apart from the frequency of this appendicular form of gastro-enteritis occurring in group 2, the incidence of true appendicitis was high during this epidemic.

Crohn (1945) noted a similar high incidence of acute suppurative appendicitis in epidemics of acute gastro-enteritis. This has also been reported by Reimann *et al.* (1945). Quigley and Contratto (1942) described four cases of acute appendicitis in 60 cases of acute gastro-enteritis; while Graham (1944) described four cases of acute gangrenous appendicitis in 500 cases of acute gastro-enteritis occurring in troops.

During the epidemic under review 29 patients were admitted with a presumptive diagnosis of acute appendicitis. In 14 the diagnosis was accepted and they were operated on. Of these, 10 had definite acute inflammation of the appendix, three had acute inflammation of the terminal ileum, and in one case generalized hyperaemia of the small bowel only was found. The remaining 15 patients were considered to have acute gastro-enteritis with appendicular symptoms. All recovered with conservative treatment. Three of them had tender sausage-shaped tumours in the right iliac fossa. The configuration and position of these tumours suggested that these patients had some degree of ileitis. Shifting tenderness was present, although there was well-marked residual tenderness in one patient. Free fluid could not be demonstrated clinically. All three subsequently developed diarrhoea.

Tenderness and spasticity of the sigmoid colon was not uncommon, and in some patients the enlarged tender colon could be palpated.

## Differential Diagnosis

The differentiation between the appendicular form of gastro-enteritis, acute appendicitis, and acute terminal ileitis was extremely difficult. Shifting tenderness proved unhelpful; it was not elicited in any of the three cases of acute ileitis which were subjected to operation. Diarrhoea occurred at some stage of the illness in 21 out of 29 patients who were sent to hospital with suspected appendicitis. In 15 this was before or at the time of admission, and in 6 it occurred subsequently. Diarrhoea occurred in 5 out of 10 patients who had acute appendicitis, and in all three cases of acute ileitis. Diarrhoea occurred in 12 of the 15 patients who were not operated on (Table I).

TABLE I

| | Diarrhoea on Admission | Diarrhoea in Week Prior to Admission | Diarrhoea in Week following Admission | No. Diarrhoea at any Time | Total |
|---|---|---|---|---|---|
| All patients referred with suspected acute appendicitis | 8 | 7 | 6 | 8 | 29 |
| Those not submitted to operation | 7 | 2 | 3 | 3 | 15 |
| Those operated on | 1 | 5 | 3 | 5 | 14 |
| Acute appendicitis | 1 | 3 | 1 | 5 | 10 |
| Acute ileitis | 1 | 1 | 1 | 0 | 3 |
| Generalized hyperaemia of small bowel only | 0 | 0 | 1 | 0 | 1 |

Rebound tenderness was present in all three conditions with remarkable constancy. Rovsing's sign was not helpful, being present in only two cases of acute appendicitis. Rectal tenderness was present in six cases of acute gangrenous appendicitis and in one case of acute ileitis. True abdominal rigidity as opposed to guarding or deep tenderness was most reliable and helpful in differentiating the three conditions, and was found only in acute appendicitis (Table II).

## Acute Ileitis

Among 14 patients submitted to laparotomy for supposed acute appendicitis were three cases of acute ileitis. This condition was recognized and described by Crohn *et al.* (1932). All three cases corresponded closely with that description.

### Case 1

A signalman aged 22 was admitted to hospital on November 26, 1956, suffering from headache, nausea, and vomiting; he had diarrhoea with generalized abdominal pain and pyrexia of 102.6° F. (39.2° C.). He received 24 g. of sulphaguanidine daily.

On November 29 he had pyrexia of 100.4° F. (38° C.), with severe abdominal pain in the right iliac fossa, and a surgical opinion was sought. He was still vomiting occasionally, but was then constipated. When examined he had no pharyngitis or generalized lymphadenopathy; guarding and rebound tenderness was marked in the right iliac fossa, but there was no rigidity of the abdominal wall, nor was rectal tenderness present on digital examination. Shifting tenderness was absent and free fluid could not be demonstrated on clinical examination. The leucocyte count was 15,000 (neutrophil granulocytes 80%, lymphocytes 15%, monocytes 4%, eosinophils 1%).

On November 30 there was no improvement in his condition, and operation was undertaken for a suspected acute appendicitis. At laparotomy some turbid free peritoneal fluid was present. The last 3 in. (7.5 cm.) of the terminal ileum was deeply congested and oedematous, resembling a thick rather perished rubber hosepipe. The involved area was sharply demarcated from the contiguous healthy caecum and small bowel. The lymphatic nodes in the vicinity of the involved ileum and the intermediate and central nodes were all discretely enlarged, firm, and pinkish in colour. The caecum was normal, but there was some peri-appendicular inflammation. The abdomen was closed without removal of the appendix or drainage of the peritoneal cavity.

Post-operatively, gastric aspiration with intravenous fluid and electrolyte replacement was instituted until December 3, when the obstructive element had subsided. After operation 2 g. of streptomycin was given daily by the intramuscular route, supplemented by 2 g. of chloramphenicol daily when oral administration was possible. On December 6 he had recovered enough to be evacuated by air to Cyprus. On December 12 he was completely symptom-free and was evacuated to the United Kingdom.

TABLE II

| Patient | Date of Operation | Clinical Findings: Temperature on Admission | Tenderness or Guarding in R.I.F. | Abdominal Rigidity | Rectal Tenderness | Rovsing's Sign | Gross Pathology: Free Peritoneal Fluid | Appendix | Terminal Ileum | Mesenteric Lymph Nodes |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Nov. 19 | 99° F. 37·2° C. | + | 0 | 0 | 0 | + | Normal | Generalized hyperaemia | Normal |
| 2 | ,, 21 | 100 37·8 | + | 0 | 0 | 0 | 0 | Acute inflammation | Normal | ,, |
| 3 | ,, 21 | 100·4 38 | + | + | + | 0 | + | ,, ,, | ,, | ,, |
| 4 | ,, 23 | 99·8 37·7 | + | + | + | 0 | + | Acute gangrenous inflammation | ,, | ,, |
| 5 | ,, 24 | 98·6 37 | + | + | + | 0 | + | Acute inflammation | ,, | ,, |
| 6 | ,, 24 | 100 37·8 | + | 0 | + | 0 | 0 | ,, ,, | ,, | ,, |
| 7 | ,, 24 | 101 38·3 | + | 0 | + | + | + | Acute gangrenous inflammation | ,, | ,, |
| 8 | ,, 26 | 102 38·9 | + | + | 0 | 0 | + | Acute inflammation | ,, | ,, |
| 9 | ,, 27 | 100·4 38 | + | + | + | − | Purulent | Acute gangrenous inflammation. Perforated | ,, | ,, |
| 10 | ,, 30 | 101·8 38·8 | + | 0 | 0 | 0 | Turbid ++ | Peri-appendicular inflammation | Acutely inflamed | Acutely inflamed |
| 11 | Dec. 1 | 100 37·8 | + | + | 0 | 0 | + | Acute inflammation | Normal | Normal |
| 12 | ,, 1 | 102·6 39·2 | + | 0 | + | 0 | ++ | Normal | Acutely inflamed | Acutely inflamed |
| 13 | ,, 2 | 101 38·3 | + | 0 | 0 | 0 | ++ | ,, ,, | ,, ,, | ,, ,, |
| 14 | ,, 5 | 99·8 37·7 | + | + | 0 | 0 | + | Acute inflammation | Normal | Normal |

### Case 2

A gunner aged 19 was admitted to hospital on December 1, 1956, with central abdominal pain which he had had for three days. One week prior to this he had had a brief attack of diarrhoea. Six months previously he had suffered a similar attack of pain, which had subsided without treatment. He had neither nausea nor vomiting, and was apyrexial. When examined he was found to have marked tenderness and guarding in the right iliac fossa. Shifting tenderness and free fluid were absent on clinical examination. Rectal tenderness on digital examination was pronounced. A provisional diagnosis of acute appendicitis was made. The leucocyte count was 16,000 (neutrophil granulocytes 75%, lymphocytes 16%, monocytes 6%, eosinophils 2%, basophils 1%).

Operation was carried out on December 1. A small amount of clear free peritoneal fluid was present. The appendix and caecum were high and bound down by dense adhesions. Only after an adherent but uninflamed appendix had been removed and the caecum mobilized was the condition of the ileum discovered. The terminal 2 in. (5 cm.) was deeply congested and oedematous, with a sharp line of demarcation separating it from the healthy ileum. The inflammatory process extended up to the ileo-caecal junction but did not involve the caecum. The mesenteric lymph nodes were discretely enlarged and congested. The abdomen was closed without drainage. Post-operatively the patient began to vomit continuously, and gastric suction with intravenous fluid and electrolyte replacement was necessary. Following operation, 2 g. of streptomycin was administered daily by the intramuscular route, supplemented by 2 g. of chloramphenicol orally on December 3, when gastric aspiration and intravenous fluid replacement were discontinued.

By December 6 the patient had recovered considerably and was fit enough to be evacuated by air to Cyprus. On December 12 he was up and about on normal diet, and was evacuated to the United Kingdom.

### Case 3

This patient, a private aged 23, was a member of the Norwegian contingent of U.N.E.F. He was admitted to hospital on December 2, 1956, with pyrexia of 101° F. (38.3° C.), central abdominal pain, and colic. He complained of nausea, and vomited repeatedly. The leucocyte count was 12,000 (neutrophil granulocytes 82%, lymphocytes 12%, monocytes 5%, eosinophils 1%).

When examined he had marked tenderness in the right iliac fossa with guarding. Rebound tenderness was elicited. Shifting tenderness and free fluid were absent on clinical examination, rectal tenderness on digital examination was marked. A provisional diagnosis of acute appendicitis was made.

At operation on December 2 a moderate amount of clear peritoneal fluid was present. The appendix was found to be normal. The terminal 5 in. (12.5 cm.) of ileum was thickened and oedematous and of a deep plum colour; the mesenteric lymph nodes were also enlarged and fleshy. The abdomen was closed without removal of the appendix or drainage. Post-operatively he was given 2 g. of streptomycin and 2 g. of chloramphenicol daily. Recovery was uneventful until December 4, when he developed mild diarrhoea. On December 7 he was well enough to be transferred to the Norwegian hospital. He was symptom-free and back to full duty on January 12, 1957.

## Discussion

Felsen (1936) followed up 400 cases of bacillary dysentery, among which 29 cases of acute distal ileitis occurred. Crohn (1949), while accepting that a condition similar to acute distal ileitis may occur during epidemics of bacillary dysentery, considered the imputation by Felsen that *Shigella dysenteriae* was the cause of acute ileitis unsubstantiated.

Reports of acute distal ileitis occur not infrequently in the literature, though usually in association with non-specific mesenteric adenitis. Rosenburg (1937) described two cases occurring among 75 cases of non-specific mesenteric adenitis. Aird (1945) also mentioned the occurrence of this condition in association with non-specific mesenteric lymphadenitis. Jackson (1937) suggested that acute non-specific mesenteric lymphadenitis and acute distal ileitis are phases of the same disease. Crohn (1949) disputed this, but thought that acute ileitis was undoubtedly an individual phase of regional ileitis capable of complete subsidence in 25 to 50% of cases. Warren and Sommers (1948) reported 15 cases of acute ileitis, 12 of which regressed, 2 progressed to the chronic phase, and 1 patient died. Rose (1946) reported three cases diagnosed and operated on for acute appendicitis. Armitage and Wilson (1950) reported 26 cases of acute terminal ileitis submitted to laparotomy in 15 years. Ten of these were followed up, and some of them had been subjected to appendicectomy. All recovered completely. They considered it unlikely that Crohn's disease began in this way.

There is obviously great variance of opinion on the aetiology and prognosis of acute terminal ileitis.

## Summary

An account of the incidence of appendicitis and acute ileitis during an epidemic of acute gastro-enteritis is given.

Some of the previous literature on acute ileitis is reviewed and three cases of this condition are described.

The patients with acute ileitis were given short courses of streptomycin and chloramphenicol, since a causal organism would neither be incriminated nor excluded. Appendicectomy was performed in one case in error. Most authorities consider appendicectomy ill advised in this condition, in view of the dangers of perforation and fistula formation.

Early air evacuation for post-operative cases was possible because a short flight at low altitude only was involved.

In the absence of laboratory investigations no conclusions with regard to aetiology in these diseases can be drawn. Nevertheless, their incidence over a period of six weeks in a relatively small population of young healthy adult males is remarkable, and does suggest that a common factor operated to produce all three conditions.

REFERENCES

Aird, I. (1945). *Brit. med. J.*, **2**, 680.
Armitage, G., and Wilson, M. (1950). *Brit. J. Surg.*, **38**, 182.
Crohn, B. B. (1945). *Gastroenterology*, **4**, 511.
—— (1949). *Regional Ileitis*. Staples Press, London, and Grune and Stratton, New York.
—— Ginzburg, L., and Oppenheimer, G. D. (1932). *J. Amer. med. Ass.*, **99**, 1323.
Felsen, J. (1936). *Ann. intern. Med.*, **10**, 645.
Graham, W. H. (1944). *Milit. Surg.*, **95**, 296.
Jackson, A. S. (1937). *Surg. Gynec. Obstet.*, **65**, 1.
Quigley, T. B., and Contratto, A. W. (1942). *New Engl. J. Med.*, **226**, 787.
Reimann, H. A., Hodges, J. H., and Price, A. H. (1945). *J. Amer. med. Ass.*, **127**, 1.
Rose, T. F. (1946). *Aust. N.Z. J. Surg.*, **15**, 184.
Rosenburg, S. (1937). *Arch. Surg. (Chicago)*, **35**, 1031.
Warren, S., and Sommers, S. C. (1948). *Amer. J. Path.*, **24**, 475.

The muscular dystrophy group of the Central Council for the Care of Cripples announces that, since its inception a little over two years ago, its members have collected over £12,000 to support research on diseases of muscle. Grants have already been made to support work in London, Oxford, Edinburgh, Newcastle upon Tyne, and Birmingham, and other applications for funds are at present under consideration. Workers engaged in studies of normal or diseased human muscle who need financial support are invited to write for information to the Central Council for the Care of Cripples, 34, Eccleston Square, London, S.W.1. The muscular dystrophy group would also be interested to hear from sufferers from muscular dystrophy, and their friends and relatives, who are not at present members.

# DISSECTING ANEURYSM OF AORTA SUCCESSFULLY TREATED BY OPERATION

BY

**PETER MARTIN, V.R.D., M.Chir., F.R.C.S.Ed.**

*Surgeon, Hammersmith Hospital and Chelmsford Group Hospitals*

AND

**JOHN D. MUIR, F.R.C.S.Ed.**

*Surgeon, Chelmsford Group Hospitals*

The successful surgical management of dissecting aneurysm of the aorta has been recorded on 12 occasions. DeBakey (1956) has reported nine, Warren, Beckwith, and Muller (1956) two, and Swann and Bradsher (1956) one, all from the United States. A further successful case is recorded here.

## Case Report

A shipwright aged 50 was at work, when he experienced a sudden severe pain in the front of his chest, radiating up to his neck. He felt very ill, but, without telling his mates, he mounted his bicycle and started for his home about a mile away. On the way his right leg became numb and felt useless, but he managed to reach home, by which time his right leg was in severe pain. He called in his doctor, who found him collapsed but conscious, with an absent right femoral pulse. The doctor considered the diagnosis of an iliac embolism and sent him immediately to hospital.

On admission he was collapsed and suffering great pain in the front of his chest, though his right leg was no longer

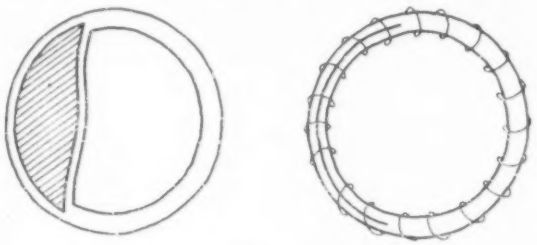


FIG. 1

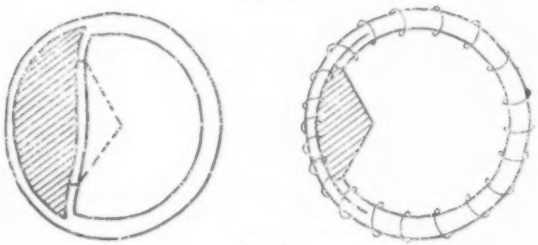


FIG. 2

painful. Clinical examination of the chest showed emphysema and chronic bronchitis. The pulse was 90 and regular; B.P. 180/110. The heart sounds, apart from an accentuated second aortic, were normal, and the heart was not enlarged. E.C.G. was normal. There were no neurological symptoms. The right leg was colder than the left, and the right femoral pulse and the pulses distal to this could not be felt.

The sudden onset of pain in the chest, followed by symptoms suggesting an acute ischaemia of the right leg together with severe collapse without significant hypotension, and a normal E.C.G., suggested a dissecting aneurysm of the aorta. It was felt that operation was urgently demanded, and this was done just three hours after the first symptom had occurred.

*Operative Procedure.*—The right common femoral artery was exposed and found to be patent. Through a right paramedian incision the aorta, its bifurcation, and the common iliac arteries were exposed. The right posterior aspect of the aorta and the right common iliac artery had a bruised discoloured appearance. The upper limit of this was not traced further than just above the inferior mesenteric artery. The aorta and upper half of the right common iliac artery pulsated fully, but there was absence of pulsation in the distal half of the common iliac and external iliac arteries. Clamps were applied and the common iliac artery was divided. The distal clamp was released and the artery was found to be obstructed by intramural clot, which was readily expressed by massage. After a free retrograde flow was established the clamp was reapplied and the intima, where split from the adventitia, was stitched back into place (Fig. 1). A segment about the size of half a postage stamp was then excised from the inner wall of the aneurysm, proximal to the point of section of the iliac artery, to allow re-entry of blood into the lumen (Fig. 2). An end-to-end anastomosis of the reconstructed iliac artery was then done. The abdomen was closed after it was seen that a good pulsatile blood flow was present through the iliac vessels.

Convalescence was uneventful; there was no further chest pain after operation, the blood flow in the right leg gave no cause for anxiety, and the distal pulses were normal. The patient was discharged home four weeks later, and was well and free from symptoms 12 weeks after operation.

## Comment

Reviews of dissecting aneurysm have been made by Shennan (1934), Creech, DeBakey, and Cooley (1956), and Warren *et al.* (1956), and reiteration would therefore be idle.

Nature's "cure" of rupture into the lumen of the aorta gives the clue to surgical treatment. It would seem proper to decompress the intramural aneurysm as high as possible—in the descending thoracic aorta just distal to the subclavian artery preferably, as most dissections start from a split in the intima just distal to the aortic valves. In the above case decompression was done in the common iliac artery and has been successful, though another case recorded in the literature, and similarly treated, was not (Gurin, Bulmer, and Derby, 1935). In those less common cases where the split in the intima occurs distal to the subclavian artery, it appears better to excise the aorta from above the split and inset a graft after suturing the intima to the adventitia of the lower thoracic aorta (Creech *et al.*, 1956). Decompression through an incision in the aorta makes difficult the approximation of the intima to the adventitia to prevent further dissection, a procedure which can be done satisfactorily only after complete transection of the aorta with subsequent resuture.

ADDENDUM.—Since this paper was written the patient has died. He lived for eight months and returned to his normal work. At post-mortem examination it was found that the artificial opening made by us at his operation was smoothed off and covered with an intima-like lining and was working efficiently. Death was due to a rupture of the aneurysm into the pericardial sac. This emphasizes what we suspected at the time—that decompression should be done at as high a level as possible.

### REFERENCES

Creech, O., DeBakey, M. E., and Cooley, D. A. (1956). *Texas St. J. Med.*, **52**, 287.

DeBakey, M. E. (1956). *Surg. Gynec. Obstet.*, **102**, 372.

Gurin, D., Bulmer, J. W., and Derby, R. (1935). *N.Y. St. J. Med.*, **35**, 1200.

Shennan, T. (1934). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 193.

Swann, W. K., and Bradsher, J. I. (1956). *New Engl. J. Med.*, **255**, 36.

Warren, W. D., Beckwith, J., and Muller, W. H. (1956). *Ann. Surg.*, **144**, 530.

# VOLVULUS OF SMALL BOWEL DIAGNOSED PRE-OPERATIVELY

BY

**ERIK CHRISTENSEN, M.B., B.S.**

*Copenhagen*

Volvulus of the small bowel is a comparatively rare condition. In Vick's (1932) collective statistics of 6,892 cases of intestinal obstruction volvulus was the cause in 176, one-fifth of them involving the small bowel. Most authors stress the difficulty of early diagnosis, and pre-operative diagnosis of this condition is so rare as to warrant the publication of the following cases.

### Case 1

A 42-year-old woman was admitted to Surgical Department A of Frederiksberg Hospital as an acute case with a history of recurrent attacks of abdominal pain after undergoing a total hysterectomy for fibroids in a gynaecological department one year earlier. Thirty-six hours before admission diffuse pains had started in the upper abdomen; her bowels had been open 20 hours before admission. During the last 12 hours the pains had moved down in the right lower quadrant, and no flatus had passed.

On examination her temperature was 38.2° C., pulse 100. The tongue was dry, and direct and rebound tenderness was elicited in the right iliac fossa with a maximum about McBurney's point. The lower midline scar after the operation showed no hernia. A pelvic examination revealed extreme tenderness on both sides, especially the right. With a preliminary diagnosis of intestinal obstruction, perhaps appendicitis, operation was decided upon. (A phone call to the gynaecological department had given information of the extent of the gynaecological operation.)

At operation the abdomen was opened through a right lower pararectal incision; large amounts of thin faecal-smelling fluid gushed out, and dilated coils of small bowel were found. After removal of the normal appendix a cystic mass the size of a grapefruit was found in the pelvis. When lifted forward it was seen to consist of a gangrenous loop of ileum, twisted twice anti-clockwise. After cutting a fresh adhesion to the left ovary, detorsion was easy. A resection of 30 cm. of small gut with side-to-side anastomosis was carried out. The post-operative course was smooth.

### Case 2

A 36-year-old woman was admitted to hospital for ileus one month after Case 1. Six months previously a supravaginal amputation of the uterus and a bilateral salpingo-oophorectomy had been done in the gynaecological department for benign disease. Since then she had had several attacks of pain in the right fossa. For three days she had been suffering from meteorism and borborygmi; her bowels had last been open 48 hours before admission. No flatus had been passed during the past 24 hours, and she had vomited three times. Clinical assessment of this case was rendered difficult because she had received several soothing injections by attending doctors at home before admission.

On examination the temperature and pulse rate were normal; the tongue was dry. The abdomen showed a lower midline scar; there was no dilatation or tenderness. A pelvic examination revealed a mobile uterine stump. With a suspicion of small-bowel volvulus—being wise after the above case—a straight *x*-ray examination of the abdomen was made. This revealed a coil of small bowel filled with fluid and air, showing air and fluid levels in the pictures taken with the patient erect: this is a characteristic picture of volvulus.

At operation the abdomen was entered through a lower midline incision through the old scar. Bloody fluid was met with. A dilated, bluish-red coil of ileum was found twisted once anticlockwise, fixed by a fibrous band to the mesentery and some smaller ones to the upper part of the old scar. The gut was freed, and detorsion was easily accomplished. As the gut was viable the abdominal wall was closed in layers. The post-operative course was uneventful.

### Discussion

Any condition causing fixation of one part of the gut while the neighbouring coil is mobile may lead to volvulus. It seems probable that a sudden filling of one segment of gut may lead to volvulus (Kerr and Kirkaldy-Willis, 1946), and peculiarities of diet may contribute to this (Kallio, 1932). According to McKechnie and Priestley (1936), the ileum is most frequently involved, especially the lower and middle parts. The gut rotates around the axis of the mesenteric artery, and a closed loop obstruction ensues. Torsion may be intermittent, but in some cases oedema and adhesions cause fixation of the rotated loop. This again leads to venous and arterial obstruction, oedema, growing dilatation, and fluid accumulation in the coil. Gangrene, perforation, and peritonitis will follow if intervention is delayed, and the mortality is high.

In the aetiology, congenital anomalies—malrotation, exomphalos, jejunal diverticula, or Meckel's diverticulum (Christensen, 1954)—may play a part. In adult persons acquired conditions—adhesions, tuberculosis, internal herniae, foreign-body impaction, tumours of the small gut (Ogilvie and Shaw, 1955)—are the cause. Torsion of the gut may also take place following gastro-enterostomy or subtotal gastrectomy (Poulsen, 1954).

Pre-operative diagnosis is very difficult. Attacks of colicky pains, vomiting with comparatively painless intervals, and tenderness of the abdomen should lead to a suspicion of volvulus. No dilatation is seen. In some cases, according to Evans and Bigger (1947), there is a definite "position of relief," as a rule on one of the sides, rarely the knee–elbow position: tension on the mesentery is relieved in this way. The *x*-ray picture is important: in about half the cases the typical arch pattern is seen, while the rest show multiple dilated coils and fluid levels in the erect films (Ripstein and Miller, 1950).

Early recognition and operation is of course imperative to counter the still too high mortality of strangulating obstruction of the small bowel.

REFERENCES

Christensen, E. (1954). *Brit. med. J.*, **1**, 1347.
Evans, E. I., and Bigger, I. A. (1947). *J. Amer. med. Ass.*, **133**, 513.
Kallio, K. E. (1932). *Acta chir. scand.*, **70**, Suppl. 21, p. 58.
Kerr, W. G., and Kirkaldy-Willis, W. H. (1946). *Brit. med. J.*, **1**, 799.
McKechnie, R. E., and Priestley, J. T. (1936). *Amer. J. Surg.*, **34**, 286.
Ogilvie, T. A., and Shaw, H. M. (1955). *Brit. med. J.*, **1**, 142.
Poulsen, O. (1954). *Dansk. kir. Selsk. Forh.*, p. 18.
Ripstein, C. B., and Miller, G. G. (1950). *Surgery*, **27**, 506.
Vick, R. M. (1932). *Brit. med. J.*, **2**, 546.

# Medical Memoranda

## A Case of Primary (Adeno) Carcinoma of the Jejunum

Adenocarcinoma of the jejunum or ileum is uncommon. Males are said to be affected twice as often as females, but collected series differ on whether the jejunum or the ileum is more frequently involved. In our case the lesion was in the proximal quarter of the jejunum. The cases are usually late in presenting, owing to the fluid nature of the contents of the small bowel, and the prognosis is poor. A resection is said to be possible in more than 50%, but the operative mortality is in the vicinity of 30% to 40%. The pre-operative correction of anaemia, hypoproteinaemia, and fluid and electrolyte deficiency should lower this figure. No more than 5% of the cases can be expected to survive a five-year follow-up. Kiefer (1933) gives the average duration of life after resection as one year, and Mayo and Nettrour (1937) as eighteen months.

### CASE HISTORY

A man aged 77 presented in the out-patient department of Queen Mary's Hospital for the East End with a history

of increasing constipation over a period of some months, recurrent episodes of colicky abdominal pain, vomiting, and temporary "stoppage of the bowel," and an indefinite loss in weight. The patient had passed no mucus, blood, or melaena stool per rectum. He admitted to symptoms of early bladder-neck obstruction and had suffered angina of effort for 10 years.

On examination he was pale, wasted, and anaemic, with De Morgan's spots on his trunk, a lipoma in the middle of the epigastrium, and an indefinite mass to the left of the umbilicus and left rectus muscle. His liver was palpable two fingerbreadths below the right costal margin, being smooth, even, and without obvious neoplastic involvement. Rectal examination showed nothing abnormal except for a clinically adenomatous enlargement of the prostate.

*Special Investigations.*—Blood group O Rh-positive. Serum potassium, 16 mg./100 ml. Serum chloride, 630 mg./100 ml. Serum sodium, 380 mg./100 ml. Blood urea, 44 mg./100 ml. White-cell count, 8,000 per c.mm. Haemoglobin, 58%. Erythrocytes, 3,090,000. Colour index, 0.96. P.C.V., 27%. M.C.V., 90 c$\mu$. M.C.H.C., 35.4%. Tests for occult blood in stools negative. Fractional test meal revealed a low gastric curve.

A barium enema was reported upon as follows. "Colon filled fairly easily and regularly. No contour filling defect

Photograph of the specimen.

seen. No organic lesion of caecum or colon seen." A barium meal and follow-through was not carried out (see below). His blood picture was improved by transfusion, and his general state by a non-residue diet supplemented with fortified foods. He was given a pre-operative course of succinylsulphathiazole, was prepared for theatre, and a laparotomy was performed by Mr. Roy Parkinson on December 5, 1956.

*Findings at Operation.*—An annular constricting carcinoma of the jejunum, which had almost completely occluded the lumen, was found approximately 18 in. (45 cm.) from the duodeno-jejunal flexure. The hypertrophy of the jejunum proximal to the cancerous stricture was striking, whilst the rest of the small gut was narrow and collapsed (see Fig.). The glandular involvement in the mesentery was such that operative cure was regarded as impossible. There were no secondary deposits in the liver and no obvious peritoneal seedlings. A resection and end-to-end anastomosis was performed.

*Pathological Report.*—The gross specimen showed an annular growth involving the jejunum. Representative sections revealed a well-differentiated adenocarcinoma whose morphology was alveolar, papilliform, and cribriform. Focal necrosis was present. There was a complete malignant penetration through the muscular coats of the bowel wall. An enlarged lymph node showed a bulky metastatic deposit of a necrotic carcinoma.

The post-operative course was uneventful and he was discharged from hospital 14 days later. When seen three and six months later there were no signs of recurrence and he felt well.

### COMMENT

Our case was not definitely diagnosed pre-operatively. The barium enema was negative, and, although this does not positively exclude colonic disease, it was thought that the cause of his recurrent obstructive symptoms did not lie in the large bowel, but rather in the small bowel. A barium meal may well have produced a diagnostic picture, but as careful and repeated radiological examination will reveal no more than 50% of tumours of the small intestine (Maxwell, Crile, and Dinsmore, 1948), and as we did not wish to run the risk of having an acutely obstructed patient on our hands, we prepared him for theatre and proceeded. The patient made an uneventful post-operative recovery.

Thanks are due to Mr. Roy Parkinson, under whose care the patient was admitted, for permission to publish the case; also to the pathological department of Queen Mary's Hospital for the East End for preparation of the sections and the photographic plate, to Dr. Woodhouse Price for his pathological report, and to Dr. O. R. Robinson, who performed the barium enema.

R. P. YAXLEY, F.R.C.S., F.R.C.S.Ed.

#### BIBLIOGRAPHY

Caris, T. N., Eisen, B., and Gilpatrick, C. W. (1955). *U.S. armed Forces med. J.*, **6**, 1371.
Fraser, K. (1945). *Brit. J. Surg.*, **32**, 479.
Kiefer, E. D. (1933). *New Engl. J. Med.*, **208**, 1042.
Maingot, Rodney (1955). *Abdominal Operations*, 3rd ed. Lewis, London.
Maxwell, E. A., Crile, G., and Dinsmore, R. S. (1948). *Surg. Clin. N. Amer.*, **28**, 1149.
Mayo, C. W., and Nettrour, W. S. (1937). *Surg. Gynec. Obstet.*, **65**, 303.
Ogilvie, T. A. (1956). *Med. Ill. Lond.*, **10**, 373.
—— and Shaw, H. M. (1955). *Brit. med. J.*, **1**, 142.
Rankin, F. W., and Mayo, C. (1930). *Surg. Gynec. Obstet.*, **50**, 939.
Rinsma, S. G., and Eggink, S. J. (1954). *Arch. chir. Neerl.*, **6**, 65.
Shallow, T. A., Eger, S. A., and Carty, J. B. (1945). *Amer. J. Surg.*, **69**, 372.

## Heat Hyperpyrexia Following a Turkish Bath

Heat syndromes are relatively uncommon in the British Isles. A case of heat hyperpyrexia which occurred in a patient taking a Turkish bath is described.

The descriptive title "heat hyperpyrexia" is confined to patients with temperatures of 107° F. (41.6° C.) or above. It may result from exposure to high environmental temperatures; from pyrexial illness, particularly malaria; or, less commonly, from thyrotoxicosis, from excessive intake of protein, or from severe muscular exercise. In all cases the mechanism is the same—namely, the inadequacy of the normal mechanism of heat dissipation, particularly sweating, to cope with the increased body temperature. Fluid and electrolyte disturbances and cardiovascular collapse may complicate the picture.

The predisposing factors include coincidental illness, alcoholism, and the wearing of unsuitable clothing in a hot environment. Subjects who have previously become acclimatized to high temperatures and who then lose their acclimatization are particularly susceptible to heat hyperpyrexia.

### CASE HISTORY

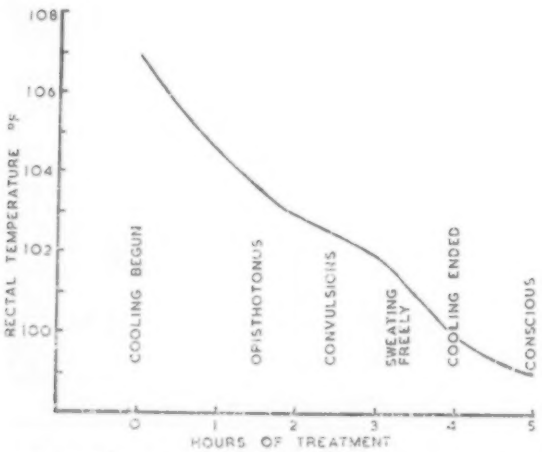
A woman of 57 was unconscious when admitted to hospital at 5 p.m. on May 30. She had gone that afternoon to the Turkish baths for the first time for about a year, although she had previously taken Turkish baths at short intervals over a period of many years. She settled in the first of the steam rooms, temperature 100° F. (37.8° C.), and began to read, but then appeared to fall asleep. After an interval of 40 minutes an unsuccessful attempt was made to rouse her. An ambulance was called and she was sent to hospital. She arrived in the ward about two hours after entering the Turkish bath.

She was an obese woman of plethoric type, height 5 ft. 2 in. (157 cm.), weight 12¾ stones (79.4 kg.). Her face was red and suffused, her skin hot and dry, and she was breathing

stertorously at a rate of 30 a minute. Her rectal temperature was 107° F. (41.6° C.); pulse rate 90, poor volume, regular; and B.P. 90/50. Her pupils were widely dilated, but contracted intermittently independent of light stimulation, and her eyes moved slowly from side to side. Her fundi were normal. The corneal reflex, cough, and swallowing reflexes were present, but she did not respond to painful stimuli. There was no neck stiffness, and the only signs in the peripheral nervous system were general depression of reflexes and of muscle tone. The plantar response was flexor. There were no other abnormal physical findings. From the history and physical findings heat hyperpyrexia was diagnosed and treatment was instituted.

Chlorpromazine, 25 mg. intramuscularly, was given to depress the heat-regulating centre and discourage shivering; she was covered with a wet sheet, and ice packs were placed around her trunk. The rectal temperature was recorded at five-minute intervals and the B.P., pulse, and respirations were recorded at 15-minute intervals.

In the next two hours her rectal temperature fell to 103° F. (39.4° C.) (see Chart), but her general condition




Rate of fall in rectal temperature and sequence of events.

appeared to have deteriorated. Her pupils were constricted and fixed and she showed a marked degree of opisthotonos. The plantar response was now extensor. She was passing voluminous watery motions continuously. A lumbar puncture revealed clear C.S.F. under 140 mm. pressure with no evidence of block in the cord. The detailed report obtained later showed no abnormality: cells, 1 per c.mm.; protein, 30 mg. per 100 ml.; sugar normal; chloride, 734 mg. per 100 ml.; Lange 0000000. There was no evidence of a cerebral vascular lesion, and the cooling process was continued. The B.P. and pulse rate had not altered significantly during this period.

Three hours after instituting treatment the patient's temperature was 102° F. (38.9° C.) and opisthotonos had passed off. She developed generalized epileptiform convulsions involving the trunk and limbs, but not the face. These occurred at intervals of one to two minutes and each lasted one to two minutes. Sodium phenobarbitone, 3 gr. (0.2 g.) intramuscularly, was given and repeated 20 minutes later, after which the convulsions became less frequent and ceased 45 minutes after they had begun. An E.C.G. taken at this point was found to be quite normal.

After four hours of treatment the rectal temperature was 100° F. (37.8° C.) and the patient was sweating freely, so the cooling process was discontinued. She now lay quite still and was breathing normally. About five hours after cooling was instituted she suddenly sat up in bed and vomited a large quantity of undigested food and apparently simultaneously regained consciousness. Her return to consciousness was very rapid, because attempts at conversation with her a few minutes before she vomited were unsuccessful.

Re-examination at this time revealed no abnormality, apart from temperature 99° F. (37.2° C.). Her B.P. had risen to 150/95. Her memory was quite clear up to the time she "fell asleep" in the Turkish baths about six hours previously, when she had had no warning that anything untoward was happening to her.

She passed no urine during the 12 hours following her recovery of consciousness, but was very thirsty and drank several pints of fluid. Diuresis was satisfactory over the succeeding 24 hours. An E.E.G. taken on the fourth day after the episode was quite normal. The blood W.R. and full blood picture were normal. She was discharged home on the fifth day.

When seen in the out-patient department two months after her discharge, she appeared to be quite well, and full physical examination revealed no abnormality. Her home doctor wrote that the patient's colleagues had noticed since her return to work (teaching) that her memory and powers of concentration were much impaired. Careful questioning in the out-patient department did not reveal any obvious impairment, and in the absence of the letter from the doctor she would have been passed as normal. However, it is possible that minor degrees of disability would become obvious only to those in constant contact with the patient.

## COMMENT

The differential diagnosis lay between heat hyperpyrexia and a cerebral vascular accident, particularly involving the brain stem. The history of exposure to heat, the hot, red, dry skin, dilated pupils, low B.P., and thready pulse, and the absence of signs of cerebral damage made heat hyperpyrexia the more likely. When the patient developed opisthotonos, lumbar puncture was performed to exclude frank haemorrhage or fulminating meningitis.

The short history of exposure is very unusual, the condition usually occurring after several days or a week of continuous exposure to heat (Malamud *et al.*, 1946; Maegraith, 1952, and personal communication). The patient said she had recovered from an upper respiratory infection two to three days before the episode. It is also notable that she had been accustomed to frequent Turkish baths and had then not taken one for a year. These facts may be cited as predisposing the patient to heat hyperpyrexia (Maegraith, 1952). The occurrence of watery diarrhoea and convulsions are both typical of the conditions of hyperpyrexia.

The prognosis depends on the effectiveness of the cooling process, and it is said that a patient with hyperpyrexia who is not cooled will inevitably die (Maegraith, 1952; Darling, 1955). Many of those who recover show residual brain damage (Walters, 1951), and the suggestion of impairment of memory and loss of concentration mentioned in the doctor's letter may well be the result of slight brain damage. Fortunately, this could not have been severe.

It is possible that the cause of the clinical picture presented was a cerebral vascular lesion, either a small thrombotic or haemorrhagic lesion, or spasm of a vessel supplying the brain stem, but the bulk of the evidence is in favour of a diagnosis of heat hyperpyrexia.

Thanks are due to Dr. T. H. Boon for his encouragement, and to Dr. R. K. McCuish for his assistance in the preparation of this paper.

J. C. STODDART, M.B., B.S.,
Royal Victoria Infirmary, Newcastle upon Tyne.

### REFERENCES

Darling, R. C. (1955). In *Textbook of Medicine*, edited by R. L. Cecil and R. F. Loeb, 9th ed., p. 518. Saunders, Philadelphia.

Maegraith, B. G. (1952). *Brit. med. J.*, **1**, 1345.

Malamud, N., Haymaker, W., and Custer, R. P. (1946). *Milit. Surg.*, **99**, 397.

Walters, J. H. (1951). *Lancet*, **1**, 460.

# Reviews

## HYPOTENSIVE AGENTS

*Hypotensive Drugs.* Proceedings of a Symposium on Hypotensive Drugs and the Control of Vascular Tone in Hypertension, held in London on April 5 and 6, 1956, at the Wellcome Foundation. Edited by M. Harington, M.B., M.R.C.P. (Pp. 222+x; illustrated. 50s.) London, New York: Pergamon Press Ltd. 1957.

A symposium on hypotensive drugs and control of vascular tone in hypertension may be of great interest to its participants, but the title does not immediately capture the attention of the rest of the profession, which may have grown rather weary of the succession of hypotensive agents introduced year after year, so that there has been little time in which to learn how to use any of them properly. Moreover, the lurking suspicion remains that we do not really know what we are doing, and that we are unlikely to do so until we understand just what essential hypertension really is. To read these proceedings in this reactionary frame of mind is salutary. The openers are mostly distinguished biochemists, pharmacologists, physiologists, or professors of medicine—very few of whom suffer from the fatigue, disappointment, and scepticism of the disillusioned practitioner or consultant who bears the brunt of the practical management of these drugs. Thus the flag of science is kept flying away from the pettifogging complaints of the sufferers from hypertension, and, donning a metaphorical white coat, the reader may sit quietly by the fireside and enjoy the mysteries of the biochemical laboratories.

The lesson begins with a remarkable chapter on the precise action of all the known hypotensive drugs by Dr. H. R. Ing. This alone would be enough to recommend the book highly. Biochemical principles relating to the action of these drugs are discussed fully by Dr. H. Blaschko, who seals the high standard of the symposium. The pharmacology of a new series of ganglionic blocking agents is described by J. W. Billinghurst, and of hydrallazine and reserpine by Dr. J. Tripod and Dr. Marthe Vogt. The pharmacological approach is maintained by Professor W. S. Peart, who discusses dibenamine and its relatives in an illuminating manner, and by Dr. J. G. Widdicombe in his account of the veratrum alkaloids. Dr. Eleanor Zaimis discusses the development of tolerance to ganglion-blockers, and A. F. Green touches on the relative selectivity of action of the diquaternary amino benzhydryl nitriles. Points of clinical interest are discussed in informative contributions by Dr. M. Harington, Professor J. McMichael, Professor F. H. Smirk, Professor G. A. Perera, Professor C. Bartorelli, and Dr. B. Hood.

The symposium ends where we might have expected it to begin, with information concerning the nature of hypertension itself by Professor Clifford Wilson; the physiological control of the peripheral resistance in normal and hypertensive subjects by Björn Folkow; and a description of experimental renal hypertension by M. A. Floyer, and of extrarenal factors by J. M. Ledingham, James Conway, R. S. Duff, and Professor Peart.

All this is very illuminating, frustrating, time-consuming, confusing, and thoroughly educational; it is in the best traditions of British medicine and the Wellcome Foundation, and the book is recommended with high praise to all interested in this very important field.

PAUL WOOD.

## PELVIMETRY

*Pelvimetry.* By Herbert Thoms, M.D. (Pp. 120. 37s. 6d.) London, Toronto, Melbourne, Sydney, Wellington: Cassell and Co. Ltd. 1957.

Any publication on pelvimetry by a pioneer in the subject as famous as Dr. Thoms must inevitably command wide interest and respect. This little book of only 120 pages, with 45 carefully selected illustrations, is admirably concise and beautifully produced. Sixteen short chapters deal with subjects as varied as the "Meaning and Accuracy of Pelvic Measurements" and "Development of the Pelvis"; "Nutrition and Pelvic Conformation" and "Abnormalities caused by Disease"; the "Clinical Significance of Pelvic Variations" and "Assimilation Pelvis"; and "Injuries to the Coccyx" or "Separation of the Symphysis Pubis." The purpose of the book is "to place before practitioners of obstetrics a practical description of variations and abnormalities of the bony pelvis in relation to labour and to describe certain diagnostic procedures by which pelvic morphology and pelvic capacity can be ascertained." For 25 years Dr. Thoms has conducted a routine clinical and radiological assessment of the pelvis of all primigravidae delivered in his unit at Yale, and the theme with which the book begins and ends is that every primigravida should have "a radiological screening" by a single inlet and lateral film. Dr. Thoms concedes that for screening purposes the lateral film can be omitted if the inlet film is correlated with a clinical assessment. The radiological technique he uses is well illustrated and described. The claim that the practice of these methods has reduced the incidence of trial labour, of difficult forceps delivery, and of caesarean section will give many readers food for thought, and some may wonder how all three reductions are possible. Perhaps the answer depends on Dr. Thoms's definition of trial labour.

The book concludes with a quotation from the 1939 prophecy of Professor Munro Kerr to the effect that pelvic radiography for primigravidae will be accepted as an essential detail in antenatal care. The question of whether this is now either necessary or desirable as a routine procedure, as opposed to a selective one for special cases, is not discussed, nor is any reference made to the vexed problem of maternal and foetal radiation hazards. Apart from these rather surprising omissions, this little book is an infant worthy of its illustrious father, and we wish them both well.

J. STALLWORTHY.

## INTRODUCTION TO PREVENTIVE MEDICINE

*Preventive Medicine and Public Health: An Introduction for Students and Practitioners.* By Fred Grundy, M.D., M.R.C.P., D.P.H. Third edition. (Pp. 309+viii; illustrated. 25s.) London: H. K. Lewis and Co. Ltd. 1957.

This book is described as an introduction to preventive medicine for students and practitioners, and the author modestly disclaims that it should be considered as a textbook. What should be the characteristics of an introduction? It must be attractive and arresting to the novice; it should deal clearly with essentials and provide a simple but cohesive picture of the subject. That is a requirement of any introduction. In this particular field it should show that a study of the illnesses and the prevention of the maladies of a population as opposed to the care of the particular individuals is a rewarding and worth-while task.

The book fulfils its object. There is an interesting and accurate description of local and central health and welfare authorities and of the essential part medicine plays in the social structure. There is a broad assessment of the meaning of health as well as an appreciation of the parts played by heredity and environment—including the growing importance of nutrition and international health. The essential function of a medical officer as an educator in health matters is stressed. The book is beautifully produced and is a pleasure to handle. The criticisms are few and not important. "Casual" should be "causal" (p. 11). I wish that the author had been able to attempt a definition of "public health by reference to a single underlying aim or principle" (p. 10). For the sake of the record it should be mentioned that the General Board of Health did not agree with John Snow's findings regarding the Soho pump, and they had reasons for not doing so. Finally, reference should be made to George Crabbe, an extract from whose work appears on page 266. These are minor criticisms. The appearance of three editions in six years is evidence of the value of this book, and it can be unreservedly recommended as a sound and interesting introduction.

LLYWELYN ROBERTS.

## HEALTH AND HYGIENE

*Health and Hygiene.* By A. Leslie Banks, M.A., M.D., F.R.C.P., D.P.H., and J. A. Hislop, M.A., M.D., M.R.C.P.(Edin.). (Pp. 322+viii; illustrated. 15s.) London: University Tutorial Press Ltd. 1957.

It is always a difficult task to write a small textbook on a big scientific subject without condensing the material so much that the work reads like a catalogue. This book, *Health and Hygiene*, overcomes the difficulty to a great extent. It is well written, and there is a new approach to history which is very refreshing; it covers a wider field than the usual Chadwick–Simon limitations. The authors, Professor A. L. Banks and Dr. J. A. Hislop, of Cambridge, have comprehended the vast area of scientific public health very effectively in a spread of 300 pages. As a rule they have been successful in balancing one subject with another, although it might be argued that the personal health services have been scamped a little. The descriptions of the environmental factors are clear and well illustrated, and the verbal accounts would be readily followed by the undergraduate who is unfamiliar with the techniques of modern public-health practices. In some chapters, especially in relation to food values and requirements, chemical formulae and simple sentences jostle one another rather closely; but, on the whole, one of the great virtues of the book is the skill with which the narrative is handled.

This textbook can be recommended with confidence for use in undergraduate medical schools and as a guide for nurses and teachers. The layman without much background of preventive medicine would read the book with sustained interest. The practising health officer and the postgraduate student would also enjoy the study, but they would have blessed the authors for a short chapter bibliography.

J. M. MACKINTOSH.

## BLOOD-PRESSURE SOUNDS

*Blood Pressure Sounds and Their Meanings.* By John Erskine Malcolm, B.Sc., M.B., Ch.B., F.R.C.S. (Pp. 93+vii; illustrated. 12s. 6d.) London: William Heinemann Medical Books Ltd. 1957.

According to the author's theory of systemic arterial resonance two shock waves originate in the left ventricle and aorta at each heart-beat. These pulse-producing forces cause two types of pressure wave throughout the arterial system, both having the velocity of sound in blood, but one being modified by the physical characters of the arterial wall. Matched resonance in the system results in a series of transient stationary waves with fixed nodes and antinodes extending from the aortic valve to the palmar arch. The first part of the book describes the experiments upon which the thesis is based and explains the production of the blood-pressure sounds. The subsequent chapters describe the applications of the theory of systemic arterial resonance to certain pathological conditions of the circulation in which persistent stationary waves may occur. Corroboration of the presence of such waves is suggested by the sigmoid arterial distortion which occurs in atherosclerosis, and the sites of deposition of calcium salts in sites of atheroma.

This book will be of great interest to research workers and clinical physiologists, and will also make interesting reading for the clinician who is concerned mainly with the circulation. It is well illustrated and there is a full bibliography.

J. F. GOODWIN.

## RED-CELL CHEMISTRY

*Chemistry of Erythrocytes: Clinical Aspects.* By H. Behrendt, M.D. (Pp. 227+xi. 43s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

This book has been written for the clinician. It attempts to give him a clinically orientated account of the chemical constitution of the red blood cell, and of the special relation of its composition to that of the plasma in health and disease. The first three chapters deal respectively with the structure, chemistry, and functional organization of the erythrocyte, its separation from whole blood (sedimentation, packed cell volume, etc.), and with the protein haemoglobin.

The succeeding six chapters—on proteins other than haemoglobin, on nitrogenous substances, carbohydrates, lipids, water and electrolytes, trace elements, and enzymes—collect whatever there is known about these and the red blood cell. More often than not they describe what has first been found in other cells and tissues and was then rediscovered with erythrocytes as the material. Thus the chapter on carbohydrates includes a figure naming the intermediates in the well-worn pathways of enzymic glycolysis in the Embden–Meyerhof cycle. The chapter on enzymes has another figure illustrating the steps in the Embden–Meyerhof scheme, showing this time, besides the intermediates, also the enzymes and coenzymes. One is somewhat reminded of the pre-1914 story of the Pole who was asked to write an essay on the elephant and produced "The Elephant and the Polish Question."

Although the book has been written for the clinician, it is difficult to see where he will find much special help or information, but biochemists, physiologists, and pathologists will discover valuable information in concentrated form. These workers may be disappointed at the sparseness of technical details in the description of methods of investigation, but they will be compensated by the liberal collection of references.

H. LEHMANN.

## CLINICAL USE OF RADIOISOTOPES

*Clinical Use of Radioisotopes: A Manual of Technique.* Edited by Theodore Fields, M.S., F.A.C.R.(Assoc.) and Lindon Seed, M.D. (Pp. 455; illustrated. 72s.) Chicago: Year Book Publishers, Inc. London: Interscience Publishers, Ltd. 1957.

Different people who are using radioisotopes in clinical work will require different sorts of information. This book is described as "a manual of technique" and as an "attempt at presentation of preferred techniques by experienced users." It illustrates both the merits and the disadvantages of this plan. On the one hand it contains a great deal of practical information on certain tests, techniques, and methods of therapy with radioisotopes, with their procedure, their normal results, and the relevant details of equipment and calculation. On the other hand it is admittedly selective both as to the subjects discussed and the methods advocated, and it is therefore easy to disagree with many of the procedures selected. The 17 contributors are mainly on the staff of Chicago or Cleveland hospitals and laboratories, although there is a useful chapter on radioautographs by Dr. Fitzgerald and one on the U.S. Atomic Energy Commission's requirements by Mr. Machurek. Much of the book deals with the design and conduct of a radioisotope laboratory, and gives useful guidance on safety precautions and clinical routine. Again, not all of the comments would be accepted by every worker in this field, but they incorporate an obviously wide experience and make useful reading. The earlier sections deal with diagnostic tests and therapeutic technique. In the former the haematological uses of $^{51}Cr$ and labelled vitamin $B_{12}$ are well described and explained, various circulatory measurements with $^{131}I$ serum albumin are discussed, and certain thyroid function tests outlined and evaluated. A short section is included on cerebral and intraocular tumour location with radioiodide or radiophosphorus. The therapeutic section is so brief that the text is in places dangerously over-simplified and dogmatic, although the section by Dr. Kaplan on cardiac therapy with $^{131}I$ is crisp and useful.

E. ERIC POCHIN.

Dr. Geoffrey Lapage has compiled an admirable account of *Animals Parasitic in Man* for the Pelican Medical Series (Penguin Books Ltd., Harmondsworth, Middlesex; 320 pp., 5s.). Although written in non-technical language, the book will be worth a place on the bookshelf of the scientist and the physician. It is well illustrated and there is an excellent index.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY FEBRUARY 22 1958

## INFLUENZA VACCINE TRIAL

The recent world-wide epidemic of influenza was unusual in many ways, not least in the unique opportunities which it afforded for large-scale trials of vaccine. The problems of influenza vaccines are recurrent: they arise not because of any difficulty in their manufacture but because of the necessity to make periodic adjustments in their make-up in order to keep pace with the continual antigenic changes in influenza viruses.[1,2] There is growing evidence that vaccines made from virus strains which are antigenically not sufficiently up to date cannot be expected to give much protection, so that each major antigenic change in the influenza virus raises once more the problems of how best to prepare and use vaccine, and how much protective effect we can expect from it. Last May, when it was known that an antigenically new variety of virus was spreading in Asia, an autumn or winter epidemic in Great Britain seemed very probable. There was thus a rare opportunity to prepare vaccine from the new Asian viruses in advance of the epidemic wave.

The Medical Research Council's Committee on Clinical Trials of Influenza Vaccine grasped this opportunity to make a scientific assessment of the protective value of the vaccine, and an interim report of their investigation appears in the opening pages of the *Journal* this week. As a first step it was necessary to see what type of antigenic response might be expected from different doses of vaccine, since previous experience of influenza vaccines was not sufficient to give a precise answer to the question. Groups of R.A.M.C. and R.A.F. volunteers were inoculated with different doses of vaccine made from a virus strain isolated in Singapore, and they were bled three weeks later to assess their antibody responses. The responses were uniformly low, presumably owing to the fact that people in Britain had not previously experienced an antigen of this kind. In support of this explanation, a second booster inoculation of vaccine produced much higher antibody titres. But just as these results became available, and before they could be fully applied, signs appeared of an autumn epidemic of influenza.

In Great Britain and elsewhere in Europe, and in the U.S.A., the unseasonal appearance of epidemic influenza some months before it normally shows itself caused some dislocation of influenza vaccine trials, necessitating last-minute alteration of plans. Nevertheless, in the present trials it was possible to obtain clear information about the protective value of the vaccines tested on some 3,000 volunteers. They had been previously recruited from residential schools, teachers training colleges, and miscellaneous centres, and were inoculated in September and early October with a single dose of one of three vaccines. The first was a monovalent vaccine prepared from the Singapore strain and tested at two different concentrations; an earlier plan to test two doses of this vaccine given at an interval of four weeks had to be abandoned because of the early onset of the epidemic. The second vaccine was prepared from a mixture of three older influenza strains, and it was included in order to see how important it was that the vaccine virus should be antigenically up to date. The control vaccine was made from influenza B virus, and it was a strict condition of the trial that neither volunteers nor those who inoculated and observed them should know which vaccine the volunteers had received. The assessment of cases was based mainly on clinical diagnosis, which should be reliable during an epidemic such as that experienced; but, in addition, laboratory confirmation of the diagnosis in some of the patients made it clear that most of the cases diagnosed must have been due to infection with Asian strains.

In many of the volunteer centres the epidemic peak occurred too early to allow any valid assessment of the vaccines to be made. In the remaining centres, however, influenza cases were beginning to occur shortly after the vaccines were given, and the assessment of the vaccines was made by comparing the number of cases which occurred within eight days of inoculation with the number occurring nine or more days after inoculation. This division is justified by the fact that vaccine would not be expected to show any protective effect within the first week of inoculation; moreover, when it was applied, clear differences emerged in the effects of the three vaccines. The Asian vaccine was estimated to cause a threefold reduction—that is, 66% protection—in the number of influenza cases as compared with the numbers in the control group occurring nine days after inoculation and thereafter. Within the first eight days after inoculation no differences were found. The polyvalent influenza A vaccine behaved just like the

[1] *Brit. med. J.*, 1957, **1**, 1517.
[2] Ibid., 1957, **2**, 38.
[3] Bell, J. A., Ward, T. G., Kapikian, A. Z., Shelokov, A., Reichelderfer, T. E., and Huebner, R. J., *J. Amer. med. Ass.*, 1957, **165**, 1366.
[4] Commission on Influenza of the Armed Forces Epidemiological Board, ibid., 1957, **165**, 2055.
[5] Culver, J. O., Nitz, R. C., and Lennette, E. H., ibid., 1957, **165**, 2174.

control influenza B vaccine, so it can be concluded that the stimulus of the up-to-date Asian antigen was necessary for protection. Recent published accounts[3-5] of trials of Asian vaccines in the U.S.A. have given figures of effectiveness in the range of 40–67%.

The figures in the M.R.C. trial are satisfactory and provide useful information for the future. In the present epidemic the disease has generally been described as mild, though, as Dr. H. A. K. Rowland points out this week (p. 422), reported death rates have varied greatly in different parts of the world. In Great Britain, as Dr. W. J. Martin shows (p. 419), deaths were not high when the large numbers of influenza cases are taken into account. But a few fulminating cases, such as those reported by Dr. D. Bruce Neilson at page 420, occurred, and it is difficult to avoid the troublesome question, What would the public have thought of the Asian influenza vaccine if a virulent epidemic had swept the country? Vaccine might have protected two-thirds of those inoculated, but the total number of people who could have been inoculated in time would have been only a small proportion of those at risk. Influenza epidemics seem to occur in cycles, and interest in influenza research waxes and wanes along with the epidemic cycles. The world-wide epidemic which we have just witnessed may yet do some good if it stimulates more research into the problem of how to protect a large population quickly against a virulent influenza epidemic.

## COLOSTOMY AND THE PATIENT

After analysing the answers to a detailed questionary given by 92 patients with a permanent colostomy, R. J. Samp[1] recently came to the following conclusions: "We of the Cancer Research Hospital, Tumor Clinic, are unanimous in our belief that a colostomy is a high but worth-while price to pay to live. We have found that the colostomy patient can adjust rapidly to his new hygienic routine, if adequate educational preparations are afforded to him prior to his discharge post-operatively. We must stress the importance of the interval follow-up examination and the opportunity for the patient to discuss the problem with the doctor." Most of the patients were aged between 50 and 70 and they were almost equally divided between the sexes. All but one had the colostomy after a Miles's resection for carcinoma of the rectum. The report is useful in showing how patients in America manage their colostomy and how they react to it.

The large majority practised irrigation of the colon through the colostomy, as a rule every day, but in some cases less frequently. However, 12% had abandoned irrigation, giving as their reasons the pain caused, the messiness of the procedure, and the increased comfort if the colostomy was left alone. Most of those who never irrigated were men, and all but one were over 60 years of age. From the answers of those who regularly irrigated certain general conclusions were drawn. Plain warm water is better as the irrigating fluid than soapy water, which leads to rapid emptying of the colon with incomplete cleansing. The use of a pint (568 ml.) of water or less or insertion of the rubber tube for a distance less than 4 in. (10 cm.) also leads to incomplete emptying of the colon.

Unintentional spilling from the colostomy was a nuisance in some patients, and the usual factor blamed was food, not its quantity but its nature, such items as cabbage, beans, raw fruit, and fats being mentioned; some patients blamed the irrigation, either the use of too much irrigating fluid or incomplete emptying. Odour from the colostomy was also sometimes a trouble, which some patients were able to lessen by not eating chocolates, sweets, and eggs, while others used perfumes or applied deodorants to the colostomy dressings.

Most of the patients were able to continue in employment and to live normal social lives, though a minority suffered in both these respects. Most found that their spouses showed understanding of their problems, and all had discussed the colostomy with them at some time. Some patients showed decreased sexual activity, but divorce as a direct consequence of the colostomy was unusual. Samp judged that most of the sexual disorders were organic rather than psychological in origin and were possibly related to decreased autonomic control resulting from the sacrifice of nerves which accompanies a Miles's resection.

The questionary is apt to be unreliable for eliciting information on personal problems, and a much more gloomy view of the effect of a colostomy is given in the report by R. B. Dyk and A. M. Sutherland,[2] also coming from the U.S.A. Perhaps the striking fact

[1] Samp, R. J., *Surg. Gynec. Obstet.*, 1957, **105**, 491.
[2] Dyk, R. B., and Sutherland, A. M., *Cancer*, 1956, **9**, 123.
[3] Gabriel, W. B., *Proc. roy. Soc. Med.*, 1945, **38**, 692.
[4] Dukes, C. E., *Lancet*, 1947, **2**, 12.
[5] Clayton-Jones, E., *Med. Press*, 1956, **235**, 551.
[6] Brooke, B. N., *Postgrad. med. J.*, 1954, **30**, 237.
[7] *Brit. med. J.*, 1957, **1**, 274.
[8] Aylett, S., *Surgery of the Caecum and Colon*, Edinburgh and London, 1954.

about both reports is the almost unquestioning acceptance of the ritual of regular irrigation of the colon. This performance was condemned by W. B. Gabriel[3] so long ago as 1945 as being unnecessary, harmful, and dangerous. Later Cuthbert Dukes[4] showed himself to be truly a clinical pathologist by deserting his laboratory to visit in their own homes 100 patients with a permanent colostomy. He found that the large majority of patients could live healthily without practising irrigation, and he made a number of other observations which make his study of great importance. The practice of regular irrigation has been vigorously attacked by Clayton-Jones,[5] who invokes the use of methyl-cellulose granules by mouth to aid the colostomy to work "naturally" at regular times. Doctors who have to advise their patients on how to live with a colostomy will find useful guidance in his articles and in one by B. N. Brooke,[6] which also includes advice on the related, but dissimilar, problem of life with an ileostomy, and some of the important points in the practical management of a permanent colostomy have previously been discussed in these columns.[7] For those patients, probably a comparatively small minority, who need regular colonic irrigation the technique is well described in a monograph by S. Aylett.[8] There can be no doubt that the efficient management of a colostomy is a matter of profound importance to those patients—and they are very numerous—who need to spend the rest of their lives with one.

## DISEASE EDUCATION BY THE B.B.C.

Dr. Charles Fletcher and Dr. John Fry—both present at the Lime Grove luncheon on February 4—differ, as their letters show, about the telecasting of live operations. Dr. Fry says it is "by no means certain *yet* that live telecasts will be made of the surgical operations mentioned." Dr. Fletcher says that if the Editor of this *Journal* had been at this lunch he would have "learnt that *no* 'live' operation is to be televised." (Our italics.) Dr. Fry was there and is still uncertain. Our representative at this informative lunch was also uncertain, for in his report to us he wrote that he gathered that films would be used "only when it is unavoidable." And in the roneoed handout there was the following item: "April 8: Negotiations are in progress with Leeds Infirmary to take live television cameras into the theatre during an operation involving the use of an artificial heart or kidney." Again, in the *Radio Times* of February 7, Mr. Bill Duncalf wrote, "the B.B.C. cannot adequately express its gratitude to them [doctors] for finding time to cope with the extra problems of live television—nor to those patients who have agreed to co-operate." The B.B.C. itself seems to have got into a muddle about it, also. In one statement[9] to the Press, evidently relying on the same handout as we have, a B.B.C. spokesman said, "We shall not be doing a live operation unless the authorities agree. . . . But we will use film where live television is not admissible." But later, according to the same account, a B.B.C. official made another statement "in which he said that in no circumstances was it intended to put a live television camera inside an operating-theatre." This fortunate second thought came the day after the leading article that was the cause of all the trouble had appeared in this *Journal*, and eleven days after the Lime Grove luncheon. The B.B.C. is now, it appears, going to get no nearer to the operating-table than the "skylight which shows the general scene." The evidence thus shows that Dr. Fletcher's chastisement is a little misplaced. He errs, too, in suggesting that the leading article was a "malicious attack upon all those members of your profession who are participating in these programmes." If Dr. Fletcher has any special interest in this series he should declare it, as plainly as we have declared our opposition to it.

And now let us turn to Dr. Fry and his more moderate criticism—entirely free, like ours, from malice. He does not accept the reference in the leader to mitral valvotomy "as strictly accurate," though he admits he did not see the film. Our representative was, most suitably, a layman who is familiar enough with medical matters and men. He did see the film. His written account of the experience was vivid and instructive. Although this was not his first medical film, at one point he and "other persons in the audience (as I found out later) were obliged to light cigarettes, look at their watches, think hurriedly of some domestic triviality—in short, resort to all the subterfuges usual in a captive audience in a state of rebellion." One of the audience apparently had to be escorted to the fresh air after the lights went up. So much for these questions of accuracy.

Opinion on the desirability of fostering an interest in disease is divided. A medical spokesman at the Lime Grove luncheon said that if a patient as a result of seeing the B.B.C. programme went to his doctor worried lest he might have cancer but only had a muscular spasm—then was it not the doctor's duty to

[9] *The Times*, February 15.
[10] *Yorkshire Post*, February 15.
[11] *The Listener*, February 13, p. 295.

relieve that kind of anxiety? Would it be malicious to suggest that it was the duty both of the B.B.C. and of the medical teams working with it *not to create this kind of anxiety*?

We believe that many doctors will echo the opinion of Professor P. J. Moir, Dean of the Faculty of Medicine at Leeds, who, as reported,[10] said, "Speaking as a surgeon I know television does show what wonderful procedures can be carried out in surgery, but to the untrained lay mind they may be quite horrifying." He thought there was already far too much talk on the B.B.C. and in newspapers about disease, and "if we now add television to dramatize disease we are further encouraging neurosis and increasing the anxiety about disease."

We doubt the propriety of doctors and hospitals taking part in the present series, without questioning their motives. The real offender in all this is the B.B.C. It is determined to make people's flesh creep, even though its television cameras have now to be removed to the skylight. In a different but cognate context the B.B.C. was taken to task in its own publication last week by its dramatic critic under the highly appropriate title "Home Horrors." An excerpt is given from an adaptation of a Simenon novel. Appropriately, it is a doctor speaking. Commenting, the critic writes[11]: "I wonder if the B.B.C. should not be ashamed to see the excerpts in print. And if they should not be more ashamed to have given them dramatic performance on the air." In the meanwhile, to fortify the public taste for the morbid and sensational, the B.B.C., on Tuesday this week, broadcast in Woman's Hour a programme called "The Unknown Seed," in which two women and two doctors took part in a discussion on artificial insemination. "To ensure privacy, their views were recorded separately in the consulting-rooms of a London specialist." Again, we doubt the propriety of doctors lending their private consulting-rooms for this kind of public entertainment. Those who may be so misguided as to take this as a "malicious attack" upon professional colleagues should listen to the layman who writes in the B.B.C.'s own publication, *The Listener*: "A public broadcasting service has not only to please its listeners. It has also to avoid, as far as is reasonably possible, giving offence."

## RESERPINE IN THYROTOXICOSIS

The thyroid hormones play an important part in regulating end-organ responses to noradrenaline and adrenaline. For example, P. Peltola[1] has detected increased sensitization to adrenaline in experimental hyperthyroidism in mice, and W. R. Brewster and colleagues[2] have shown in dogs that many of the haemodynamic and metabolic changes of thyrotoxicosis are not directly due to the activity of the thyroid hormones but rather to the increased effects of adrenaline and noradrenaline. Many of the clinical features of thyrotoxicosis can be explained on this basis.

Reserpine relaxes the nictitating membrane in animals, and in man causes bradycardia, hypotension, and increased secretory and motor activity of the gastrointestinal tract. These effects are due to depression of the sympathetic autonomic impulses to the respective organs. The site of action of the drug is not known with certainty, but A. J. Plummer and colleagues[3] have produced evidence that reserpine does not act peripherally. The most likely region at which the drug affects autonomic balance is the hypothalamus, where it could also give rise to the changes in emotional response which are observed clinically.[4] Depression of hypothalamic function might also diminish the production or release of thyrotropic hormone by the pituitary[5] and in this way reduce the activity of the thyroid gland.

These theoretical considerations together with the known beneficial effects of reserpine in the control of agitated hyperactive patients[1] have led J. J. Canary and colleagues[6] to study the usefulness of the drug in the treatment of thyrotoxicosis.[7] They found that the drug given orally in doses of 0.25–1 mg. 6- to 8-hourly for two to fifteen weeks did not significantly depress thyroid activity as measured by the uptake of radioiodine or the blood levels of protein-bound iodine. They were therefore unable to confirm the view that reserpine influences the amount of circulating thyrotropic hormone. Their results are consistent with those of R. V. Ford and colleagues,[7] who found no change in the uptake of radioiodine in hypertensive patients treated with reserpine. On the other hand they did find some clinical improvement in most of their cases, while in a few all symptoms and signs disappeared. The goitre, however, was unchanged in size, and, though the degree of exophthalmos remained the same, lid retraction and lag were strikingly diminished. Estimations of basal metabolic rate were carried out before and after treatment in only six of the ten patients who were treated, and in only two of these did the final value fall below +20%. Reserpine appears, therefore, to have little effect on the raised oxygen consumption of the thyrotoxic patient. In the patients to whom reserpine was given orally the clinical improvement obtained, while definite,

[1] Peltola, P., *Acta med. scand.*, 1951, **140**, 34.
[2] Brewster, W. R., Isaacs, J. P., Osgood, P. F., and King, T. L., *Circulation*, 1956, **13**, 1.
[3] Plummer, A. J., Earl, A., Schneider, J. A., Trapold, J., and Barrett, W., *Ann. N.Y. Acad. Sci.*, 1954, **59**, 8.
[4] Kline, N. S., ibid., 1954, **59**, 107.
[5] Greer, M. A., *J. clin. Endocr.*, 1952, **12**, 1259.
[6] Canary, J. J., Schaaf, M., Duffy, B. J., and Kyle, L. H., *New Engl. J. med.*, 1957, **257**, 435.
[7] Ford, R. V., Livesay, W. R., Miller, S. I., and Moyer, J. H., *Med. Rec. (Houston)*, 1953, **67**, 608.
[8] Foote, E. S., *Brit. med. J.*, 1955, **1**, 1192.
[9] Marley, E., and Pare, C. M. B., ibid., 1956, **1**, 267.
[10] Rea, E. L., and Fazekas, J. F., *Arch. intern. Med.*, 1955, **95**, 538.

was less than might have been expected with an effective antithyroid drug. Their gain in weight was not dramatic, particularly in view of the possibility that fluid retention might account for it.[8,9] In another ten subjects the drug was given intramuscularly in doses of 2.5–5 mg. 6- to 12-hourly for one to sixteen days. Distressing symptoms and signs were relieved, in some cases within 24 to 48 hours, but toxic effects were common and doses as high as these have been shown[10] to produce unpleasant and even dangerous side-effects.

Reserpine cannot be recommended as the sole therapeutic agent in cases of thyrotoxicosis, and its place as an adjunct to treatment remains to be defined. From the evidence at present available it would appear that, in the oral doses recommended by Canary and colleagues,[6] its most promising application might lie in its simultaneous administration with radioiodine. The absence of any effect on the uptake of radioiodine allows both drugs to be given at the same time, and a more rapid control of symptoms than with radioiodine alone might be expected. Many patients nowadays receive reserpine in the treatment of hypertension or for psychotic states, and it is worth remembering that the drug may suppress some of the symptoms and signs of thyrotoxicosis.[6] Thyroid function is best assessed in such patients by radioiodine studies or by estimations of the protein-bound iodine.

## STUDYING HEALTH

The London School of Hygiene and Tropical Medicine has never been slow in adapting its teaching to the needs of the day. One method which has proved its worth in recent years is the study of special subjects by groups of students taking the D.P.H. course. Last year, for instance, one group investigated the habits and health of London cab drivers, and the results are recorded in the School's annual report.[1] There is a low rate of sickness absence in this trade, which is marked by its strongly independent character. The relationship between the cab driver and his employer is an exceptional one, in that the driver is more of a bailee than an employee—that is, the cab is entrusted to him while it is plying for hire. In spite of the apparent good health in the trade the study group thought there was enough evidence to justify a wider-scale investigation into the incidence among cab drivers of chronic respiratory conditions, psychosomatic diseases, and haemorrhoids. Another group of students tried to find out if there was any readily ascertainable relationship between journeys to work and matters related to health. The wear and tear of a long daily journey, often with changes from trains to buses or to the underground, is commonly thought to be prejudicial to health. But in two of the three places of work investigated by the students no statistical association was found between days absent or times late and length of journey to work. The third inquiry—conducted among young people in Dagenham—did, however, suggest that there was a slight tendency for those who travelled further each day to lose more days off work.

Unhygienic handling of food is a common matter of complaint, and another study group at the London School of Hygiene scrutinized the booklets, pamphlets, posters, and filmstrips which are available for the instruction of the public in general and of food handlers in particular. The students concluded that the English publicity material lacked punch compared with similar productions from Canada and the U.S.A. In their view instructional programmes on radio and television were too infrequent. This study group found plenty of films and filmstrips about the correct handling of food, but none on incorrect handling: so the students produced their own six-minute colour-film on how not to handle food.

Another subject chosen for special study was chronic bronchitis, which the report describes as "still a major and almost entirely British disease." Comparing a series of middle-aged, male, chronic bronchitic patients with a control series, the group found the following factors appeared to be associated with the disease: crowding during childhood, poverty and low social class of previous generation (based on occupation of patient's father), town dwelling, work for eleven years or more out of doors, and smoking 20 or more cigarettes a day before the onset of illness. The impact of teaching by investigation is shown by the concluding words of this part of the report: "Students were impressed by the desperate seriousness of chronic bronchitis in some middle-aged men, by the extent of nursing care needed at home, and by the continued search for costly patent medicines which characterized the home life of certain sufferers."

## DELAYED EFFECTS OF RADIATION

Lack of knowledge about the delayed toxic effects of nuclear and allied radiations is disturbing. Not only is the quantitative relationship between the radiation dose and the incidence of any given effect in doubt, but even the range of possible effects that may occur is ill-defined. Any information, therefore, obtained from the study of human groups either accidentally irradiated or exposed for medical purposes is of value. In March, 1954, the detonation of a "nuclear device" over the Pacific resulted in the accidental exposure to radioactive fallout of the 82 inhabitants of two atolls in the Marshall group of islands. Immediate steps were taken by the American authorities to deal with this incident and to institute medical care, and the islanders have since been kept under close observation. From time to time reports of this survey have been issued,[1] and the most recent describes the findings two years after the accident.[2]

The 64 inhabitants of Rongelap atoll are estimated to have received whole-body radiation doses of about 175 r, and the 18 inhabitants of Ailingnae doses of about 69 r. No deaths have occurred which can be

[1] London School of Hygiene and Tropical Medicine, *Report on the Work of the School for the Year 1956-1957.*

attributed to radiation, but a number of features characteristic of radiation exposure were noted. Many of the Rongelap inhabitants developed gastro-intestinal symptoms within 24 to 48 hours of exposure, and the lymphocyte, neutrophil, and platelet counts of both groups fell to quite low levels. These changes were more marked in the more heavily exposed group, and the lymphocyte fall was greater in children than in adults. Skin contamination by the fall-out led to the development after about two weeks of epilation, patches of pigmentation, and areas of dry desquamation which in some cases went on to full moist desquamation. Analysis of urine samples showed that such radioactive nuclides as $^{90}Sr$, $^{141}Ce$, and $^{144}Pr$ had been ingested. Six months after exposure the lymphocyte and platelet counts were still abnormally low, nor had they returned, like the neutrophil counts, to control levels after a year. A review of the situation two years after the accident does not suggest that the affected populations have been unduly prone to epidemic diseases, and there has been no evidence of impaired fertility or undue complications of pregnancy. No abnormalities have been reported among children born after the accident. Both the lymphocyte and platelet counts continue to show some depression, and radioactive nuclides continue to be excreted in the urine, but in quantities well below the presently accepted maximum permissible levels. A new feature, however, is evidence that the growth of male children has been impaired. Nine boys between the ages of 3 and 15 years were compared with matched unexposed children from Majuro atoll, and the irradiated boys showed a mean deficiency in height of 2.1 in. (5.3 cm.) and in weight of 7.2 lb. (3.3 kg.). A comparison of girls failed to show a significant difference between the irradiated and control children. Although the numbers involved are very small, the differences are probably real, since W. W. Greulich, C. S. Crismon, and M. L. Turner[3] reported similar findings in the irradiated children of Nagasaki and Hiroshima. These authors believe this effect to be the result of a variety of causes, including the economic and social consequences of any profound disruption of the way of life. It is therefore doubtful whether the change noted in the Marshallese is a specific radiation effect, and the fact that it was seen only among boys is in keeping with other findings of Greulich[4] in Guamanian children that boys are less able than girls to withstand unfavourable environmental changes.

Further reports on the irradiated Marshallese will be anxiously awaited in the coming years, as, judging by experience in Western European populations, the group has only now entered the period of maximum risk from acute leukaemia. So far as other tumours are concerned, particularly perhaps skin tumours, the period of greatest risk of the clinical development of a tumour may not start until some ten to fifteen years after exposure. Finally, and particularly in the case of leukaemia, the population at risk is extremely small; even though the probability of developing the disease may well be increased for each member of the group, it is quite possible, considering the rarity of the disease, that no actual cases will be observed. Failure to observe a case of leukaemia in this group of people should not therefore be interpreted as evidence for the existence of a threshold dose of radiation for the induction of leukaemia.

[1] Cronkite, E. P., *et. al.*, *J. Amer. med. Ass.*, 1955, **160**, 430.
[2] Conard, R. A., *et al.*, ibid., 1957, **164**, 1192.
[3] Greulich, W. W., Crismon, C. S., and Turner, M. L., *J. Pediat.*, 1953, **43**, 121.
[4] —— *Amer. J. phys. Anthropol.*, n.s., 1951, **9**, 55.

## CONTROLLING DRUGS IN HOSPITAL

One of the consequences of the National Health Service has been that nurses move from one hospital to another much more frequently than formerly. For a nurse to spend her career in one hospital, or even one hospital group, is now exceptional. It is therefore a great help if every hospital has the same kind of procedure for storing and handling dangerous drugs, one that will be familiar to the nurse whatever hospital she has come from. A report issued this week by the Ministry of Health[1] gives suggestions on the control of dangerous drugs and poisons. As it points out, accidents in hospitals with these drugs are fortunately rare: "Comparatively few members of hospital staffs have personal experience of an accident with poisons in the ward, and fewer still have ever had to deal with a drug addict." Thus the rules, in successfully preventing accidents, run the risk of diminishing at the same time the attention to them that an accident so dramatically focuses. An uncommon sense of personal discipline remains inseparable from medical and nursing practice, a fact not always appreciated by those who judge these professions from the outside.

Another reason for reviewing the rules for handling poisons springs from the large number of new drugs introduced every year. Some of these, though exceedingly potent, are not classified as poisons or dangerous drugs until they have been in circulation for some time. The committee that produced this report therefore recommends that the pharmacist or consultant should have discretion to decide whether any of these drugs should be treated as Schedule 1 poisons within his hospital. In view of the special danger to children of many drugs not ordinarily thought of as poisons, a subject much explored in the last few years, the committee emphasizes the need to ensure by verbal warning and labels that drugs issued to out-patients must be kept out of children's reach at home. The committee also recommends extending the use of special bottles for poisonous liquids, so that all liquid preparations not intended for oral or parenteral administration and issued to out-patients or for use in the hospital should be in bottles fluted vertically with ribs or grooves. Finally, the abbreviations P.R.N. (*pro re nata*) and S.O.S. (*si opus sit*) were found on inquiry to be so ambiguous in intention and interpretation that the committee recommends they should no longer be used.

[1] *Control of Dangerous Drugs and Poisons in Hospitals*, Report of Joint Subcommittee on the Control of Dangerous Drugs and Poisons in Hospitals, Ministry of Health, H.M.S.O., 2s.

# MEDICAL ART SOCIETY'S EXHIBITION

BY

MERVYN LEVY, A.R.C.A., M.R.S.L.

The Medical Art Society's sixteenth annual exhibition opened on February 13 at Walker's Galleries, 118, New Bond Street, where it will remain until March 5.*

## Colour Galore

Many of the exhibitors seem to have spent their holidays at places abroad where there are abundant sunshine and colour—or so it would appear, superficially. But Mediterranean "colour" in particular is a pitfall. Here, where the brilliant sun burnishes the ultramarine and emerald waters of Cannes and Monte Carlo—here, cry the doctors, is colour: dazzling, joyous colour with a vengeance. And so there is—of a kind. But even Raoul Dufy, who perhaps more than any other painter of modern times soaked up the colour of the Mediterranean scene, even he had to reconstitute this riotous blaze. Too often the human additions to it clash with Nature's chromatic scheme. The red roofs, the shimmering pink and yellow façades of the buildings, and the many other points of pure colour with which humanity seeks to enliven the natural scene inevitably appear at times discordant since they are not planned as an intrinsic part of the total result. What seems at first a colourful scene may be in fact a natural harmony disrupted by a number of crude, out-of-key colour notes; and when the artist tries to lock it up in some permanent form his picture fails miserably to make aesthetic sense. There is no integration, no harmony, only discord. Once the whole is committed to canvas, the bright flashes of man-made red and yellow that seemed so exciting in the living scene look as cheap as the colours in a trashy Christmas card.

Dufy made peace out of this conflict by toning down the brilliance of *all* the colours involved. Very often, too, he turned the vehemence of natural and human colour into a delicate harmony of pastel shades. What he *never* did was to accept the scene as it stood. He always re-created it through his own selective, painter's eye. Doctor painters might well consider Barnsley or Wigan for their next painting holiday—preferably when it is raining. At present the Continental scene seems a little too rich for the eyes of those accustomed to the drab but co-ordinated harmonies of the British landscape.

## Pick of the Show

This year perhaps it is the sculpture section that steals the show. Outstanding are two pieces by G. Konstam. His "Fallen Horse" is superbly conceived and he has brilliantly co-ordinated the anatomical features of an extremely tricky posture. So also has he in his torso "Air Borne" (Fig. 1). I have never seen the dynamic rhythms of a torso in flight—as at the climax of a particularly energetic and graceful ballet dancer's leap—better expressed. The anatomical and aesthetic aspects of this splendid conception are blended with great knowledge and restraint. It is so easy to over-anatomize the male torso in action—a trap into which even Michelangelo often fell. Jakub Rostowski is another sculptor whose work it is always exciting to see. His subject matter, drawn straight from the whirlpool of mental illness, displays a feeling of profound identification and sympathy with the tragedy of the sufferer. This is especially so in his study "Depression." A gaunt, bowed figure, with long bony hands, appears to be playing a piano; but the hands, I imagine, are simply wandering in melancholy agitation over the keyboard of a depressive psychosis. The emaciation of the figure is symbolic perhaps of the devouring nature of such an affliction, and the whole conception suggests that gradually the flesh and bones will fall away, leaving only the malady itself.

FIG. 1.—"Air Borne" by G. Konstam.

Of the oil paintings, I thought B. N. Brooke's "Calvary" quite the best. Unfortunately it does not lend itself to photographic reproduction. In this picture Brooke has used symbolism to express an idea of the meaning of the Crucifixion. The scene, I suppose, is after the Crucifixion, since it shows an empty, glowering landscape with three bare crosses on a distant hillside. In the foreground there are two huge, beautifully painted plants. One is floating gently upwards, with its roots exposed, while the other is firmly implanted. The symbolism surely indicates both the transfigurative and ascendant qualities of the Christian faith, and the strength of its message in the temporality of the world.

B. Lux contributes a luxuriant "Spring in Surrey"; G. E. Loxton a tiny painting, "Flowers," executed with a rich, fleshy impasto; Harold Hewitt a strangely disquieting "Day Before Demolition"; Sir Harold Gillies a curious conception of "Agra From the Taj Mahal," in rich plums and sugar-icing whites and grey; and Phoebus Tuttnauer three paintings in his own inimitable manner, of which "The Lonely Robin" (Fig. 2) is perhaps the most satisfying. In the water-colour section T. Anderson's "Orchard—Impington" and "November Foreshore" are notable for the sheer exuberance of the artist's technique, while Sir Philip Manson-Bahr's "Polegate—Sussex" is a most charming and delicate portrayal of a typically English scene.

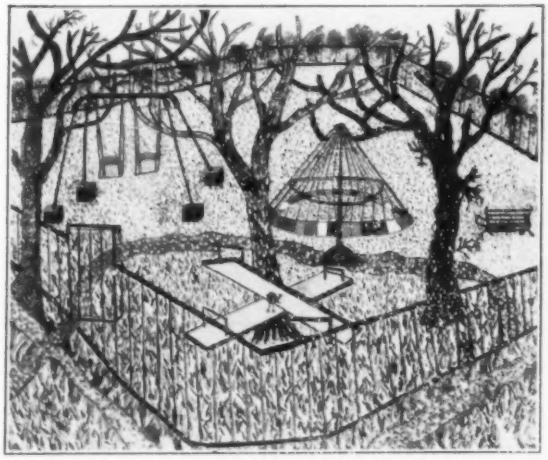


FIG. 2.—"The Lonely Robin" by Phoebus Tuttnauer.

The photographs are by Photo Studios Ltd.

*Hours of admission are 10 a.m. to 5 p.m on weekdays and 10 a.m. to 1 p.m. on Saturdays.

# INSURANCE ASPECTS OF BRONCHITIS AND ASTHMA

On February 5 Dr. J. L. LIVINGSTONE, physician to King's College Hospital and the Brompton Hospital, addressed the Assurance Medical Society on "Asthma and Bronchitis in Relation to Life Assurance." After reviewing the incidence, aetiology, and pathology of the two conditions, Dr. Livingstone discussed the clinical assessment of the bronchitic and the asthmatic, with special emphasis, in view of his audience, on prognosis.

## Size of the Problem

The incidence and mortality from bronchitis seemed to depend on two factors, said Dr. Livingstone—climate and atmospheric pollution. In dry sunny climates bronchitis was rare, whereas in the British Isles it caused much invalidism, accounting for 7% of deaths from all causes. The death rate in England and Wales was three times that of Belgium, six times that of Germany, 15 times that of France and Scandinavia, and 36 times that of the United States. The Registrar-General's figures depended on the accuracy of death certification, but, in spite of the difficulties in deciding the primary cause of death in long-standing conditions such as bronchitis, the annual death rate from the disease had remained fairly constant since 1945, at about 30,000 per annum; of these, 20,000 were classified as chronic bronchitis and 10,000 as acute or not specified. Bronchitis was the commonest respiratory cause of death, comparable figures in 1953 for pneumonia being 21,000, for cancer of the lung 16,000, for tuberculosis 8,000, for influenza 6,000, for asthma 3,000, and for bronchiectasis 2,000.

In 1949 42% of those dying of chronic bronchitis did so between the ages of 50 and 70, and 52% over that age. The essential cause of death in chronic bronchitis was emphysema, associated with progressive loss of alveoli and hence of the capillaries, resulting in decrease of respiratory reserve.

Asthma was also very prevalent in Britain. Stocks had estimated in 1949 that 1% of the population of England and Wales suffered from it, and this was probably a conservative estimate. Acute status asthmaticus accounted for most of the 3,000 deaths attributed to asthma each year. But probably many of the asthmatics who died later in life as a result of emphysema were certified as dying from bronchitis or cardiac failure. Of the deaths attributed to asthma 96% occurred after the age of 30, but 54% of them between the ages of 30 and 60. The mortality curve for asthma followed closely that of bronchitis with its rise in the winter months and in certain years, and, as in bronchitis, infection played the predominant part in causing death. The "middle-aged infective type" of asthma carried a particularly serious prognosis.

## Clinical Assessment for Life Assurance

Despite the increasing tendency amongst insurance offices to insure substandard lives, when a diagnosis of "chronic bronchitis and emphysema" was made the policy was either heavily loaded or the proposal declined. In this group of substandard lives there was perhaps a place for good clinical judgment to make more accurate diagnosis, so as to exclude the bad risks and allow a good guess at the prognosis in the remainder. In pulmonary tuberculosis the risk of breakdown was in the first few years after clinical arrest, whereas with bronchitis and asthma the risk increased with age. In the doubtful case a few years' observation was needed before a final decision, but if possible the proposal should be accepted on special conditions or business would be lost. A detailed clinical history, supplemented by the private medical attendant's report, was usually the most important factor in assessment.

In the physical examination early clubbing of the fingers was a serious sign. The type and range of chest movements was obviously important and the expansion should be measured at the level of the fourth rib and at the xiphisternum, the examiner watching for the "old soldier's" trick of contracting the shoulder-girdle muscles. The presence of wheezing which persisted after coughing to clear the bronchi might mean something more than smoker's catarrh, and if unilateral the patient should be seen on another day. Moist rales or crepitations were not found in simple bronchitis or asthma.

The proponent should be asked to bring a morning specimen of sputum; and in addition he should be made to expectorate at the time of the examination. If these specimens contained mucopus, infection was present with all that that implied, and obviously further sputum specimens must be examined to decide whether the infection was transient or persistent. Fluoroscopy was helpful in showing the range of diaphragmatic movement, the size of the heart and great vessels, and in excluding gross radio-opaque pulmonary lesions. A radiograph of the chest would not show emphysema until the late stages, but it was an essential investigation and a valuable record for future comparison.

## Respiratory Function Tests

There were now fairly accurate tests to measure the three functions of respiration—the bellows action or ventilation of the lungs; the mixing of gases in the lungs; and the diffusion of gases across the alveolar walls to and from the blood stream—but at present these tests were not sufficiently standardized and there were not enough laboratories for them to be used routinely.

An ordinary spirometer could give quite useful information on the ventilation of the lungs. The first test was the forced vital capacity (the maximum volume of gas which can be expired following a maximum inspiration, the expiratory phase being accomplished as rapidly and forcibly as possible). The forced expiratory volume at one second was probably a better measurement, however; this should be over 75% of the normal vital capacity. There was also a simple, portable, and accurate peak-flow meter, designed by Dr. Charles Fletcher and made by Ferrari's Ltd., which gave the expiratory flow rate. This was closely comparable to the maximum breathing capacity long recognized as the most practical simple test of ventilatory function. The test could be repeated after an inhalation of 1% isoprenaline solution, which diminished bronchospasm; if there was then no marked improvement in the test result emphysema was probably present, though the converse did not necessarily apply, as emphysema and bronchospasm were often combined. Only if the volume expired was up to the normal figure for age and height could emphysema be ruled out. There was no simple standardized exercise test that was generally accepted, but by watching the patient's breathing after he had walked up two or three flights of stairs the examiner had some idea of the respiratory reserve.

The medical examiner was then in a position to assign the proponent to one of three classes: (1) The bad cases which should be declined or very heavily loaded; (2) the good group acceptable for endowment policies to 55, 60, or 65 years; or (3) the doubtful group requiring observation over, say, two to five years to judge their progress.

## Conclusion

In the insurance of bronchitics the crux was the mortality rate after the age of 50—i.e., 13% up to 60 years; 30% up to 70, and 50% thereafter. Whole life policies would require a high premium; but endowment policies maturing at ages varying from 50 to 65 years, depending on the assessment of the individual case, might well be recommended. The policy could be extended if progress was favourable. In asthma the risk of death from status asthmaticus began at 30. But the risk of added infection and therefore of

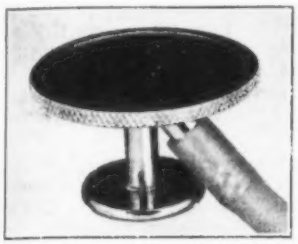
emphysema became considerable in later life, and these cases should be dealt with like the bronchitics over 50.

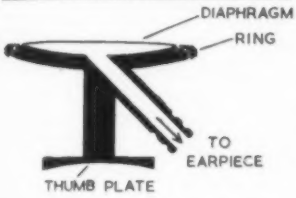
Looking 30 years ahead, said Dr. Livingstone in conclusion, control of infection by antibiotics, steroids, and other drugs, and diminished air pollution, should together make for a better prognosis in both bronchitis and asthma.

# Preparations and Appliances

## IMPROVED STETHOSCOPE CHEST-PIECE

Professor W. W. MUSHIN, of Cardiff, writes: Noting the efficiency of stethoscope chest-pieces of the diaphragm type, I made an attempt, with the assistance of Mr. Hillard, senior technician in my department, to improve on them by exaggerating what appeared to be their important features. The chest-piece illustrated resulted from trial and error. The dimensions are such that the diaphragm at its centre is only 1/16 in. (1.6 mm.) from the outlet. Silicone rubber tubing (outer diameter, 8 mm.; inner diameter, 6 mm.) connects the chest- and ear-pieces. The clarity and loudness of the sounds transmitted by this chest-piece are striking. The dimensions of the chest-piece and the specification of the diaphragm and rubber tubing are somewhat critical. The details will be supplied gladly, but the complete instrument can be obtained from Chas. F. Thackray Ltd., 10, Park Street, Leeds, 1.






# Motoring News

## IS THE MINIATURE CAR AN ECONOMIC PROPOSITION?

Within the past twelve months more and more miniature cars made in Great Britain and the Continental countries have come on to the market. There is still no British counterpart to the French Citroen 2CV, and the more miniatures one sees on the roads the more one tries to compare each of them with this 2CV, undoubtedly the best current example of the light car. But what should the buyer expect from his new miniature car? Will it really be economical, what standards of comfort will it offer, and is it worth the initial outlay? To answer all these questions one must consider the kind of work the car is to be asked to do, whether comfort is really so important, whether its novelty value will wear off quickly, and many other details.

To compare the economies of a true miniature car with those of the small conventional four-seater saloon: the former gains on tax, insurance, and petrol, but for approximately £150 more the conventional saloon offers reasonable comfort for four persons with luggage space under cover, will stand more hard wear, can be more easily serviced locally (an obvious asset for any doctor), and will depreciate less than the unconventional miniature. Against this must be set higher running costs, but in the long run the differences between the miniature and the conventional car in petrol economy are not very great. Few of the baby cars give much more than 65 m.p.g. if they are to offer reasonable speed and comfort for purposes other than just shopping, and the mass-produced saloon, now a very competitively priced article, can offer close on 50 m.p.g. if carefully driven.

Considering these little cars individually, we find the best sellers in this country are the Goggomobil, the B.M.W. Isetta, and the Heinkel, all from Germany. The most popular is the Heinkel, which at £395 is one of the cheapest and most attractive models available. It is powered by a 198 c.c. single-cylinder four-stroke engine with enclosed chain drive to gearbox and single back wheel, while a folding roof, single-piece front door, and space for two rather tiny children behind the main seat make it popular with young couples or those with only very young offspring. The B.M.W. Isetta has four wheels and a rear-mounted engine between the closely spaced rear wheels. The Goggomobil uses a 293 c.c. twin two-stroke unit also mounted integrally with the gearbox and final drive, and, with all independent suspension and excellent road holding, this is perhaps the most interesting of all the miniature cars. It costs £495 or £505 with folding roof; a de-luxe coupé model of very attractive appearance and with pre-selector gearbox is also available, but this will set you back £625, the cost of a Morris Minor or a Ford Prefect.

A recent model to come from the Continent is the Fiat 500. Produced by one of Europe's largest car factories, the new 500 is a successor to the still popular Fiat Mouse, or Topolino, designed in 1935 and put on the market in 1936. I must confess, however, that I was disappointed in this new model, which was heralded as an even more advanced model than its predecessor. Certainly the latter was ahead of its time in 1936, but the present 500 is not much faster, no more comfortable or economical, and less silent than the older model, and at £556 it is too expensive. The model 600, however, is much better value and is more luxurious.

Britain does not lag too far behind in the development of these tiny models, for we have the Meadows Frisky, the Berkeley, Bond, Unicar, A.C. Petite, and others which all offer cheaper motoring. Unfortunately we are still in the era of the two-stroke engine and the chain drive, which are outdated and noisy features, though we are ahead of our rivals with fibreglass bodies. Mass production of miniature cars is, however, still a long way off, and until this happens we cannot hope to have such models in the showrooms at sensibly low prices.

Continental manufacturers have always favoured the very small car, and they have considerable experience in designing and marketing them, so that they are reasonably comfortable and sell at low prices. The Fiat 500, for example, sells in its native Italy for less than £300, at which figure it is superlative value, whereas in Britain the Bond Mini-car is the nearest rival at £279, an austere runabout if ever there was one. The British motorist expects much more comfort than the average Frenchman or Italian, who seems content to cram five or six adults into the tiniest 7 h.p. saloon, and therefore the little two-stroke car has a hard job over here to combine comfort and dignity with economy and low purchase price. Import duty and purchase tax combine to force up the price of small foreign cars entering this country, but they are selling in quite reasonable numbers, particularly the low-powered full-sized car like the 2CV which will take a family in comfort and still give 60 m.p.g. If a car of this sort is ever marketed here then the true miniature will become redundant unless it can be sold at under £200 and give economical motoring in the region of 100 m.p.g.

At present, therefore, it seems that the conventional saloon is still more suitable for the professional man than the ingenious miniature. But improved models will continue to invade the market, with the result, perhaps, that at some future date every house will have its "bubble" car just as it now has its refrigerator or washing machine.

IAIN GELLATLY.

# Correspondence

## Disease Education by the B.B.C.

SIR,—The leading article on the televising of medical programmes (*Journal*, February 15, p 388) raises a number of important public and medical matters of principle which deserve wide and careful consideration and discussion. The first matter is whether the public deserves to be medically educated. Is there a need for informing the public—and this includes young and old as well as the so-called intelligent adult—on matters of medical interest? If one is to judge by the popularity of the medical columns in the press and of the *Family Doctor*, then it seems that the public is very deeply interested in medicine. This interest has always been there, but more so recently, when it seems to be a part of a general awakening of interest in all scientific matters. Another reason for fostering this public interest is that a knowledgeable public is an important factor in attaining and maintaining high medical standards. The public should be encouraged to be able to discriminate between good and bad medicine, and in this proper instruction is important.

If one accepts that education of the public in matters of health and disease is necessary, then this education should be carried out by the written word of the press, by the spoken word on the radio, and by the new and increasingly popular medium of television. Television is here to stay and all our past ideas and ideals must be made to fit in with it. It is a new, young, and exciting medium of social intercourse and its techniques are still rather tentative and experimental, and this applies to its medical ventures just as much as its lighter programmes. Those responsible for these programmes are learning continually on the best means by which the public is to be educated, instructed, and entertained, and in this they need the assistance and co-operation of the professions. Past programmes have laid stress on disease and have produced certain reactions in the public. In my own experience these reactions on my own patients have been those of interest and reflection. I have not encountered the anxious and hypochondriacal patients referred to. Even assuming that these latter do come and consult their family doctors, then surely even the so-called hypochondriacs are in need of treatment, and, if others are stimulated to attend, then this in itself may lead to early diagnosis of preventable diseases.

The televising of "live" surgical operations is a much more controversial matter on which there are definite ethical objections, but it is necessary to keep a proper perspective. In the programme under discussion it is, I understand, by no means certain yet that live telecasts will be made of the surgical operations mentioned. In the publicity on this programme there is reference to only two occasions when televising of actual live operations is mentioned—the possible use of an artificial heart or kidney, and possibly an operation on the brain—in all other surgical programmes films are to be shown. Films of surgical procedures have been shown in the past on the public screen and on television without arousing any ill effects. It also seems unlikely that the procedures to be televised "live" will be as dramatic as is suggested. The reference to the extract of the film on mitral valvotomy that was shown to journalists at the press conference held on February 4 cannot be accepted as strictly accurate. I was present at this conference, and, although I did not actually see the film, I listened to the comments of the lay journalists who saw it. Those who spoke all praised its clarity and stated that there was nothing in it likely to curdle the blood of potential viewers. There was certainly no comment in public by these journalists on any syncopal reactions in themselves. We will have to reserve judgment until we have seen more of this series, but this week's programme on poliomyelitis seemed full of interest and free of any events likely to worry even the squeamish.

I would agree very much with your comments on the past and present contexts of B.B.C. medical programmes. There has been too much stress on "disease," "hospitals," and "research." There is a need to inform and educate the public on health, prevention of disease, and on the common and everyday conditions that are seen in general practice and from which the majority of us suffer. Colds, coughs, bronchitis, rheumatism, boils, care of the young and aged, and so on are live, interesting, and far from undramatic. Perhaps the powers that reside in Lime Grove and Wood Lane will consider this.

Whatever criticisms are levelled at the B.B.C. in all these respects, these criticisms merely show the needs for some closer co-operation between the profession and those officials responsible for these programmes. The next rational step would surely be for the B.B.C. to set up an advisory committee with representatives from the various Colleges and other professional bodies to work together in using the medium of television to the best advantage in educating and instructing the public on medical matters.—I am, etc.,

Beckenham, Kent. JOHN FRY.

SIR,—Your leading article (*Journal*, February 15, p. 388) on the B.B.C.'s present series of television programmes "Your Life in Their Hands," although apparently directed against the B.B.C., is in fact a malicious attack upon all those members of your profession who are participating in these programmes. You accuse them of imposing upon their patients to appear "at anxious moments," of providing the public with "real blood-curdling treats," of "making people's flesh creep," and all this with the intent of "heightening people's anxiety about the state of their own bodies." Before you wrote these accusations might you not have got into touch with some of the participating doctors and inquired about their real motives and about the precautions they had taken to ensure that their patients would not be distressed and that what was to be said and shown would be acceptable to viewers? I understand that you were invited to a press conference attended by many of these doctors, at which these questions could have been asked if you had wished to discover the answers. At this press conference your views on the advisability of showing the film, to which you object, would have been invited. It appears that you did not attend, for had you done so you would have learnt that no "live" operation is to be televised in this series and that no television camera will enter any operating theatre. Might you not also have troubled to discover something about what is known of viewers' reactions to medical programmes instead of assuming that they must all be bad? In relation to the "Hurt Mind" programmes you accuse the B.B.C. of sending "very large numbers" of persons to their doctors to inquire about electric shock treatment, but you make no reference to the inquiry that was conducted before and after the series. This showed a significant change in attitudes of those who had seen the programmes—towards increasing confidence in psychiatry and decreasing fear of and revulsion from mental illness. In any case, even if the result of the programmes had been as you suggest, might not some of those who inquired about electric shock treatment have been in need of some help? Could their doctors justly complain if they sought this help from them? What are doctors for? You must also have known, though you do not refer to the fact, that this series was supported by the National Association for Mental Health and was designed to do just what you advocate—to encourage healthy thinking and a proper attitude towards prevention as well as cure.

In your article you make no reference to the large numbers of programmes on television that have been and are directed to preventive medicine—programmes on smoking, burns, weight reduction, normal pregnancy, child care, and so on. I agree that it is within this field that television can play its most useful part in relation to medicine, but I cannot agree that programmes on medical procedures or treatment, in or out of hospital, should be

banned. To keep medicine an inviolate mystery behind closed curtains is as likely to induce misery and fear in those who may have to penetrate this curtain as is confident discussion and demonstration of what goes on in hospitals. There is much to be argued on both sides, and the truth must lie in a wise compromise. Such a compromise is unlikely to be attained by your prejudiced approach—prejudiced because you reach your verdict without having seen the evidence. I cannot defend the present series, for, like you, I have not seen them as they will appear. It is too much to hope that they will be above all criticism, but I do hope that such criticism will be sensible, unemotional, and combined with approval where this is merited. More than this, I hope that you may come to realize the vast power for good possessed by television. This good will only come if doctors will study the medium and give the B.B.C. constructive advice rather than abuse. There is indeed a danger that your attitude will discourage the cautious and leave future programmes (which there will inevitably be with popular demand as it is) in the hands of the unscrupulous.—I am, etc.,

Richmond, Surrey. C. M. FLETCHER.

*** The above letters are referred to in a leading article at p. 449.—ED., *B.M.J.*

## Breast-feeding

SIR,—I feel sure that the breast-feeding survey undertaken by the Obstetric Medicine Research Unit at Aberdeen and described in your issue of February 8 (p. 310) will be studied with interest by all those engaged in the work of caring for mothers and babies. The opinion arrived at by the Unit, that "we should help in every way possible the women who wish to breast-feed, but we are not justified in putting pressure on those who are unwilling or appear to be unable to breast-feed efficiently," no doubt will be received with varying degrees of opposition and agreement. As one who has over a period of forty years been interested in this difficult and important subject, I should like to offer some remarks. I congratulate the three members of the Research Unit in arriving at the opinion that, whatever else was preventing successful breast-feeding (and the number of adverse factors considered by the Unit are legion), infantile dyspepsia, overfeeding, and "something wrong with the milk" have been completely discounted. This indeed is a happy advance in the appraisal of the problem. On the other hand, the carefully obtained evidence brought out in this survey demonstrates quite clearly that a major reason for failure is hunger resulting from the mother being unable to produce sufficient milk and the infant being unable to obtain it, and it has been towards this objective that the Research Unit concentrated their attention in their endeavour to find an explanation for so much failure in maternal feeding.

This has been mainly a "follow up" investigation, and the evidence sought after was obtained within the home and from parents and relatives. I cannot help feeling that, if it had been possible for the Research Unit to have started their survey within the maternity units during the hospital phase of breast-feeding, then valuable evidence might have been forthcoming to explain the reasons for so much subsequent failure in breast-feeding. I have myself suggested from time to time as forcibly as I can my belief that the established nursing regulations—e.g., four-hourly twenty-minute feeds, and the still prevalent idea that newborn infants are in danger of overfeeding, which many maternity units still religiously stick to and teach—can quite well be a major reason for early failure. So often these past breast-feeding rituals lead to chronic partial starvation, persistent crying, nervous upset, and exhaustion of both mother and infant, followed by the final decision to have done with them. I am convinced that why the infant finally takes a turn for the better is because the parents and relatives decide to take the feeding into their own hands and throw overboard these irritating rituals and time schedules which have been enforced by the welfare, nursing, and medical professions and have finally decided by "hook or by crook" to see to it that the baby gets the food it keeps asking for, and certainly one way of doing this is to resort to the bottle and making sure that there is an adequate hole in the teat. Like so many of our hospitals, maternity units are handicapped by shortage of staff, and no doubt some system of regularity and ordered direction is necessary in order to avoid chaos, and many of our feeding rituals have been put into practice by worried matrons and sisters in their endeavour to teach established principles on sound lines. But these rules and regulations are really now a thing of the past and should be reviewed by our obstetric and paediatric personnel. At any rate, I myself am not acquainted with any sane paediatrician who supports such ideas as "four-hourly twenty-minute feeds" and the belief in the danger of overfeeding.—I am, etc.,

Leeds, 1. C. WILFRED VINING.

SIR,—Mr. Hedley J. B. Atkins's study of the possible transmission of mammary carcinogens by human milk, alluded to in his paper on the transmission of maternal antibodies (*Journal*, January 25, p. 187), is a model for long-term research. Whilst this hypothesis remains untested, however, mental reservations about the whole-hearted advocacy of breast-feeding may also remain. It would be unfortunate if the equally "widely canvassed" possibility that satisfactory breast-feeding positively influences later personality development were lost sight of on this account. Many psychological theories (variably supported by clinical and experimental evidence) place great importance on the early mother–child relationship and "psychosomatic" contact of the nursing situation to the development of maternal instinct, and to the child's subsequent emotional integration. Since psychological illness carries such a high morbidity if not mortality risk in contemporary life no plausible speculation can be ignored.

Certainly the advocacy of breast-feeding on the grounds of reduced liability to childhood infections is less tenable than previously—as is demonstrated by Mr. Atkins's study. Robinson's[1] extensive study of children born some 20 years ago showed increased mortality, morbidity, and case mortality rates in the bottle-fed infants, so that perhaps the reduced differential risk demonstrated in recent surveys reflects in part a trend due to improved living conditions, hygiene, medical care, antibiotics, etc. It is a pity that we will have to wait so long for a scientifically ideal answer to the carcinogen dilemma. "Another 50 years" is a long time for doubt. Horne's[2] demonstration of a similar incidence of "absence of breast-feeding" in 88 patients with confirmed breast cancer as in 86 gynaecological control cases cannot be dismissed perfunctorily, particularly since he took "never having received any human milk" as his criterion and made every possible attempt to verify his data. As an interim verdict the case against breast-feeding—if not discredited—is at least not proved.—I am, etc.,

London, S.E.24. I. PIERCE JAMES.

REFERENCES
[1] Robinson, M., *Lancet*, 1951, **1**, 788.
[2] Horne, H. W., *New Engl. J. Med.*, 1950, **234**, 373.

## Management of Pulmonary Emphysema

SIR,—One statement in your annotation on the neurological aspects of pulmonary emphysema (*Journal*, February 1, p. 272) cannot be allowed to pass unchallenged. Your suggestion that 5% carbon dioxide in oxygen for 15–20 minutes every hour be used in the treatment of patients with respiratory failure is not only inept but positively dangerous. The breathing of 5% carbon dioxide by normal people for any length of time is disagreeable, and 10% carbon dioxide breathed for over 10 minutes produces unconsciousness and respiratory depression, with an alveolar carbon-dioxide level which cannot be more than 10% (inspired) + 5.6% (normal alveolar), or 15.6%. In fact it would be less than this owing to some degree of hyperventilation.

In emphysema with respiratory failure the carbon-dioxide retention has arisen because the patients are unable to ventilate sufficiently to clear out of their lungs the normal carbon-dioxide production of the body, and because at a later stage the respiratory centre has largely lost its ability to respond to increasing tensions of carbon dioxide. A number of these patients have been so anoxaemic that there

is an added anoxic depression of the respiratory centre. It is likely, therefore, that the breathing of 5% carbon dioxide would raise the alveolar and tissue carbon dioxide by almost the whole added carbon-dioxide tension (5% carbon dioxide = 37 mm. carbon dioxide partial pressure moist). The mean carbon-dioxide tension of the arterial blood (and therefore effective alveolar air) of a recent series of cases of this type reported by Westlake[1] was 70 mm. Hg, and in our own cases 72 mm. Hg tension. In our own cases the administration of *oxygen alone for 10 minutes* produced a rise of carbon-dioxide tension such as you describe to a mean of 85.3 mm. Hg partial pressure. The addition of a further 37 mm. Hg partial pressure would raise the alveolar carbon dioxide to 120 mm. Hg partial pressure, or 16.8%. Your therapy, Sir, would result in all the patients becoming comatose, and many would not recover.

Our own practice is to give oxygen by oxygen tent for up to 50 minutes in the hour, together with broad-spectrum antibiotics and treatment for the heart failure if present. The sisters and nursing staff show great skill in recognizing the tell-tale twitchings and drowsiness which precede the onset of coma and require the rolling up of the tent for a short period. The patient responds to the transient respiratory stimulus of anoxaemia during this period by vigorous ventilation with removal of carbon dioxide, and becomes less drowsy and more alert. The short periods of anoxaemia have never given rise to anxiety, and this regime will tide the patient over until antibiotics control the acute infection which is almost always the precipitating cause of the condition.—We are, etc.,

LINDSAY DAVIDSON.
Birmingham, 15. K. W. DONALD.

REFERENCE

[1] Westlake, E. K., *Brit. med. J.*, 1954, 2, 1012.

SIR,—I should like to comment on the last two statements of your timely annotation on the neurological aspects of pulmonary emphysema (*Journal* February 1, p. 272). One is pleased to see the increasing acceptance of mechanical methods in the treatment of respiratory insufficiency, but it is desirable that they should disturb the patient as little as possible. Might I suggest that even in unrelieved coma an air-tight mask (such as supplied with the Bennett intermittent positive-pressure machine) is as satisfactory as an endotracheal tube? Furthermore a characteristic of respiratory insufficiency is the repeated response to treatment, particularly when it is precipitated by infection. Thus it is difficult to understand why you recommend that mechanical aids "should not be undertaken lightly" in coma. Particularly is this advice inappropriate if one adopts the above simple procedure.—I am, etc.,

London, W.12. D. G. MASSEY.

## Informal Admission of Mental Defectives

SIR,—As one who has the overall supervision of some 600 mental defectives under guardianship I am very much in agreement with the letters of Dr. W. A. Heaton-Ward and Dr. M. P. Nelson (*Journal*, February 8, p. 338) regarding the recommendations of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency. It would almost appear that in an endeavour to avoid the alleged stigma of mental defect the Commission tries to pretend that there is really no such thing. Could anything be more absurd and illogical than to credit mental defectives with sufficient powers of judgment to decide whether or no they should remain under supervision and control? Obviously if they are so capable they are not mental defectives—and vice versa. From a fairly extensive experience of such patients as are under guardianship I can only say that if compulsory powers are abolished and adequate control is thereby rendered impossible very few people will be willing to undertake the responsibility of giving them a home and taking care of them. Furthermore, to release from compulsory control defectives, both from institutions and from foster homes, will almost certainly result in many social complications, including an increase in sexual crimes—not to mention an increase in the mentally defective section of the population.—I am, etc.,

Hove, Sussex. W. N. MAPLE.

SIR,—I have the fullest sympathy with both the worries of Dr. W. A. Heaton-Ward and also his work in the field of mental deficiency. I only regret that in his letter in your issue of February 8 (p. 338) he shows no deeper understanding of that public sentiment in regard to compulsory detentions that he tends to scout. Does he appreciate, for instance, how far his "modern concept" of mental deficiency as a "social incapacity" differs from the ordinary member of the public's concept of mental deficiency—as something based solely on defect of intelligence? Does he appreciate the basic tenet of public relations that, in order to get wholehearted public support and co-operation in the implementation of legislation, it is necessary for this first of all to be in intelligible form and, secondly, to be explained in easily understood form? If the community gives powers over the liberty of the individual, it feels itself entitled to understand why it is giving them. The necessity for such explanation does not seem, unfortunately, to have been appreciated in the working of the Mental Deficiency Acts: and the present position is a sorry example of the misunderstanding that ensues.

It is an extraordinary thing that, in all the debates prior to both the 1913 and 1927 Acts, and the discussion on mental defectiveness that accompanied them in Parliament, there appears no definition of "mind"—this was left to the experts, the medical profession. They have up to date not made a particularly good job of it, for the course of events of which Dr. Heaton-Ward complains shows that a negative definition—a declaration that "defect of mind is not of necessity defect in intelligence"—does not suffice. It immediately, and not without reason, arouses the suspicion of those whom he terms "the 'Civil Liberty' Guards."

Up to the present time this interpretation of the law has worked by virtue of the fact that the lay public in general, and Parliament in particular (as was obvious in the recent debate on the Royal Commission's Report), did not understand what was being done. This state of affairs is now, however, altering. There are three main reasons for this, all of which, it seems to me, must be understood if Dr. Heaton-Ward's anxiety is to be met. The first is that the medical profession, in exercising its prerogative as to the definition of mental defect, did not appear itself to grasp that it was dealing with two quite separate conditions: that the "social incapacity" of the so-called feeble-minded patient is something entirely different from the defective intelligence of the mentally subnormal, and consequently needs treating differently and in different circumstances. A medical superintendent, for instance, understands the reasons for an Honours B.A. being found as a detainee in a mental defective colony, but the general public do not: nor, as a matter of fact, do I. The second is that, just as patients differ, so do doctors. Certifying doctors have shown differing opinions as to what they regard as social incapacity to an extent which has, on occasions, defied the common sense. The third is the report of the Royal Commission with its formal recognition of the difference between the "psychopath" and the "mentally subnormal." This recognition, which merely expresses the present position in more realistic terms, has come to stay, and is likely to be embodied in coming legislation.

It is, of course, the "psychopathic" patient that Dr. Heaton-Ward has in mind: and in approaching fresh compulsive legislation for this type of person it seems to me that discussion in Parliament will centre on two things. First towards obtaining adequate and readily understandable definition of a psychopath—nor are M.P.s to be appeased by the knowledge that psychopaths have already been detained for years under the "pseudonym" of "high-graded feeble-minded." Second, in deciding whether, in giving powers of detention, these should be in the form of indefinite sentences, dependent solely on the decision of medical authority, or sentences for definite periods of "preventive

detention" by a lay court in circumstances where medical treatment and supervision can be given.

Always provided that clear and open decisions emerge from these discussions, Dr. Heaton-Ward will no longer have to wake up on Sunday morning fearing to open his newspapers.—I am, etc.,

House of Commons. DONALD MCI. JOHNSON.

SIR,—I would like to refer to the letters of Dr. W. A. Heaton-Ward and Dr. M. P. Nelson in the *Journal* of February 8 (p. 338). It is agreed that the modern concept of mental deficiency is that of social incapacity of such a degree as to render an individual in need of care, supervision, and control for his own protection or the protection of others. I believe that it is not necessary in every case where hospital admission is required to have legal powers of detention to obtain these ends.

With many severely handicapped mental defectives, the need for hospital care and treatment has been agreed and desired by the parents and their medical advisers both outside and inside the hospital. The patient, by virtue of the degree of defect, may not be able to make any valid observations as to whether or not he wishes to come into hospital, but this is no reason to assume that he does not. Indeed, his attitudes when in hospital compared with his previous history suggest he is happier in hospital. That it should be necessary in such a case to involve a judicial authority and obtain an order to regularize his stay in hospital is cumbersome, an embarrassment to parents, and may engender or aggravate feelings of guilt over the admission of their offspring. Under the present Acts, even if the case were placed under Section 3, the Order would still have to be reviewed at intervals by the Visiting Justices.

The attitude of the other grades to stay in hospital, though important, is only one of the factors which must be taken into account in deciding the suitability or otherwise for informal admission. Attitudes of parents, home environment, behaviour disorders, the patient's mental make-up, must be taken into account.

As far as de-certification of patients at present under Order is concerned, the same set of criteria would seem appropriate in deciding whether or not de-certification should be recommended. After all, de-certification still rests with the Board of Control. Whilst it may be that the number of cases suitable for de-certification, or new cases suitable for informal admission, may be less than anticipated in some quarters, this in no way belittles the value of being able to admit suitable cases without formality. The ideal way to obtain hospital treatment for a mental defective is on an informal basis. Since the introduction of these informal admissions, the only justification for obtaining compulsory powers to detain such a person in hospital must rest on the fact that he requires care and treatment of a kind that is available only in hospital, is not available through other agencies, and it is essential for him, or for society, that he obtain care and treatment which he is unwilling to accept on an informal basis. I would add that since Circular (58)5 came out I have felt much happier about a number of cases discharged under (56)25, who might break down again and would come and ask us to help them. We can now do so without waiting for them "to become a subject to be dealt with."—I am, etc.,

Birmingham, 14. L. J. SEGAL.

## Carcinoma of the Breast

SIR,—In your leading article on carcinoma of the breast (*Journal*, February 1, p. 269) it is suggested that a local mastectomy can only prudently be performed for palliative reasons, and that the Edinburgh method has not succeeded in establishing itself. Although it is probably true that more radical mastectomies are being done to-day than locals, it is also probably true that an increasing number of surgeons now prefer the latter, supplemented by radiotherapy. Certainly this is the case in the area served by the Radiotherapy Unit of the Royal South Hants Hospital. Recently the results of "operable" cases in this area have been surveyed for the years 1946–54, the relative five-year, cancer-free, survival rates being calculated by the Life-Table Technique. The figures are very similar if the age group 49–69 only is considered.

*Five-year Cancer-free Survival Rates*

| | Stages 1, 2, and Not Staged | | Stage 1 | | Stage 2 | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | Hb | % |
| Radical ± Radiotherapy | 614 | 54 | 256 | 65 | 246 | 43 |
| Local + ,, .. | 432 | 67 | 221 | 77 | 160 | 59 |

The two surgical methods have been used concurrently, in the main by the same surgeons, and the same radiotherapy technique and doses, and the same criteria for staging, have been applied to both groups.

An interesting finding has been that, if cases with local recurrences in the scar area and the axilla and with no other simultaneous metastases are excluded, the five-year results are improved by only 3% in the radical operation cases and by only 4% in the local. It seems more profitable to think in terms of not causing dissemination of the disease than of preventing its local recurrence.

It cannot be argued from the figures in the table above that there is no place for the radical operation. Indeed, it may well be that the extent of the operation and the reliance placed on radiotherapy should depend on the behaviour and the general histological type of the tumour.—I am, etc.,

Southampton. A. G. C. TAYLOR.

## Influenza Vaccination

SIR,—Recently I inoculated 27 members of the staff of Victoria Hospital, Accrington, with Asian influenza vaccine, prepared from influenza virus A/Singapore/1/57 at the Wright-Fleming Institute of Microbiology, London. Twenty had two doses of 1 ml. of vaccine by deep subcutaneous injection into the left upper arm with an interval of a month between the injections. Seven had only one injection. Twenty-four of the subjects were female and 3 male; their ages ranged from 19 to 48 years. The following reactions were noted:

| No. of Subjects Experiencing: | After First Injection | After Second Injection |
|---|---|---|
| Local pain of varying intensity .. .. .. | 27 | 20 |
| Pain radiating in whole of left arm .. .. .. | 4 | 1 |
| Headache .. .. .. .. .. .. | 1 | 1 |
| Vomiting lasting 24 hours .. .. .. .. | 1 | 0 |
| Common cold (onset within 24 hours; lasted 3-5 days) | 5 | 2 |
| "Encephaloid reaction" (headache, vomiting, emotional instability with excessive laughing and crying without any apparent cause; onset within 18 hours; lasted 36 hours .. .. .. .. | 1 | 0 |

This is an extremely small trial from which to draw conclusions, and it is admittedly difficult to prove that the onset of the common cold and the "encephaloid reaction" were really due to vaccination. However, it suggests that the question of reactions from influenza vaccine needs looking into carefully before the vaccine is used on a wide scale.

I wish to express my thanks to Dr. A. L. McAdam for allowing me to submit this report.

—I am, etc.,

Accrington. S. S. JHAVERI.

## Scabies on the Increase?

SIR,—I was interested to read Dr. Allan Bigham's letter (*Journal*, February 8, p. 338) about the increase of scabies. Following a similar letter by Dr. F. F. Hellier (*Journal*, November 10, 1956, p. 1117) the research committee of the College of General Practitioners decided to make scabies notifiable within the Research Register of the College. Between March and December, 1957, I have had 87 notifications from 22 general practitioners. A progress report has

been published[1] which shows a higher incidence in females and children, and in clean homes than in untidy or dirty.—I am, etc.,

Writtle, Essex. J. C. GRAVES.

REFERENCE

[1] *J. Coll. gen. Practit.*, 1958, **1**, 83.

### Post-influenzal Depression

SIR,—A few months ago I replied to correspondence in your columns concerning the use of methylpentynol ("oblivon") in premedication (*Journal*, September 14, 1957, p. 642). I have since had some experience of a derivative of this drug, methylpentynol carbamate ("oblivon-C"), used to combat depression. During the past months when cases of influenza have been pandemic, symptoms of depression and debility have often developed. A current advertisement in the press declares that a beverage containing ethyl alcohol "works wonders," but methylpentynol in these winter months can be the physician's choice to hasten recovery and maintain employment. Methylpentynol, according to Trotter,[1] can increase concentration and confidence and relieve tension.

The majority of my cases of influenza developed similar convalescent complications: lack of confidence; tiredness; loss of appetite; and, in two to three cases out of every ten, a degree of depression. Of these, a series of 37 cases of depression following influenza have been listed, and all were treated with methyl pentynol carbamate. They were classified as "established" (mild and moderate) cases and severe cases. There were 21 males, of which 18 were "established" and 3 severe cases, and 16 females, of which 14 were "established" and 2 severe.

With the onset of convalescence, depression was apparent and symptoms were those of lack of concentration, vertigo, irritability, and fear of inability to work. Methylpentynol carbamate was prescribed in doses of 200 to 300 mg. three times daily. In the mild cases response was rapid, 200 mg. twice daily only was needed and the patient requested to return to work in three or four days. In the moderate cases 200 to 300 mg. was required two to three times daily. Response was immediate but required longer therapy—one to two weeks. The five severe cases considered received similar treatment, 300 mg. three times a day, reducing to 200 mg. twice a day, but these cases were seen more frequently and rehabilitation required from three to four weeks. Again it was interesting to note that in these advanced cases definite progress towards recovery was evident immediately following administration of methylpentynol carbamate. (One case, a female still absent from work after six weeks, now elects to return next week: two other cases not listed and believed to be established cases of depression following influenza did not respond, but both were found to have past histories of psychosis.)

There were no disturbing side-effects. Methylpentynol carbamate is slightly excreted through the lungs and occasionally an unpleasant after-taste may occur in a minority of cases. Patients forewarned of this possibility complained little, and any distaste was overshadowed by grateful appreciation for relief already being obtained. Other cases of established depression (not following influenza) are also being treated with success—e.g., menopausal cases with or without hormone therapy, shock following bereavement, and cases of varied degrees of depression arising from social problems in the home.

In my opinion, in all the above cases timely and adequate therapy with methylpentynol carbamate definitely shortened the recovery time. The patients are at once more relaxed and hopeful, they shed their fears, and with a little encouragement pick up their tools and are glad to find themselves back at work.—I am, etc.,

Orpington, Kent. R. M. HARRISON.

REFERENCE

[1] Trotter, P., *Lancet*, 1954, **2**, 1302.

### Artificial Insemination

SIR,—A.I.D. has had a big write-up in the past few months, both in the lay and, to a lesser degree, in the medical press. A lot of abuse has been directed at the donors, while little or nothing has been said in their favour. Since the donors cannot speak for themselves I feel that a few facts should be put on record about these much-maligned men. As I meet them they are married men with families of their own, who donate with the knowledge and consent of their wives; moreover, they do this for no financial reward whatever and often at considerable trouble and inconvenience to themselves. They are not sexual perverts commanding huge fees for their services. They do not regard themselves as a race of supermen, but on the other hand they are not prepared lightheartedly to cast their seed to the wind; they need to trust the doctor who deals with the matter and be assured that the couples asking for A.I.D. are meticulously vetted before being accepted, and are indeed childworthy. The couples for their part must be able to expect good health and sound mentality in the donors. It is no easy task to build up a suitable panel of donors of suitably varied types, and the sort of cheap abuse that has been thrown about recently does nothing to help but may well deter some who want to help—men who genuinely feel distressed for those couples who are denied children and who agree that it may be better for the wife to bear her own child rather than adopt one of completely unrelated parentage.—I am, etc.,

Crediton, Devon. MARGARET C. N. JACKSON.

### Preparation of Skin for Electrocardiography

SIR,—I have been following with interest the scientific discussions in your correspondence column arising from Dr. James Maxwell's letter (*Journal*, October 19, 1957, p. 942) on the preparation of skin for electrocardiography. A year ago while setting up for a cardiogram in the depths of the country I found that this time it was the electrode jelly I had left in the office. So I used "vaseline," with excellent results, and, to quote an advertisement of my youth, "since then I have used no other," or rather had not until a detail man sold me something in a "squeeze bottle" for a dollar and a quarter which is almost as good.

However, what I think is not appreciated by people taking cardiograms is the great difference in skin resistance between individuals. On some patients one can obtain low electrode resistance using almost anything; on others (the minority) the most careful skin preparations still leave a residual 60 cycle (50 to you). This is best appreciated when trying to read really low voltages as in an electroencephalogram. By the way, I know vaseline is an excellent insulator. That is why we use it on wet battery terminals.—I am, etc.,

Freeport, Nova Scotia. EDWARD LLEWELLYN-THOMAS.

SIR,—I have read with interest the letters by Dr. James Maxwell (*Journal*, October 19, 1957, p. 942), Dr. D. D. Vora (*Journal*, November 30, 1957, p. 1307), and Dr. Donald Whitfield (*Journal*, December 7, 1957, p. 1369) under the above heading. I, for one, was under the impression that the use of any special jelly in the preparation of the skin is now obsolete. When I had my "cardiopan," manufactured by Phillips-Liechtie (Switzerland) in 1951, the electrodes supplied with the instrument were encased in a piece of flannel, and the manufacturers' instructions were to soak the electrodes in ordinary tap-water and apply straight on to the patient's extremities. The chest piece also was encased in flannel, and I have never had to use either special jelly or "K-Y jelly" on any of my patients. Needless to say, I have always had excellent results.—I am, etc.,

Nairobi. B. P. ARYA.

### Tetanus

SIR,—I was interested to read Dr. D. D. Johnstone's account of tetanus in Nigeria (*Journal*, January 4, p. 12). It is not often a paper based on such a large series of personally treated cases appears in a home journal. A summary of some observations made in another comparatively large series of 77 cases of tetanus treated in India[1] may serve to emphasize some of the points made by Dr. Johnstone.

Excluding cases which gave no definite history of injury or other source of infection, our series showed a slightly closer relationship between a short incubation period and mortality than did Dr. Johnstone's series. However, his analysis, correlating incubation period and period of onset, is a timely and striking, if silent, reminder that such prognostic

criteria should be seriously assessed when considering the institution of relaxant therapy. Such treatment may still carry with it a considerable risk, though it undoubtedly has heralded in an era of hope for the hitherto hopeless case.

Dr. Johnstone questioned the value of antitoxic serum in treatment, and showed from his series that the mortality rate was not seriously affected when antitoxin was withheld. The figures of our series are perhaps even more striking: though in no case was antitoxin completely withheld, the standard dose was considerably reduced in the later cases. Of 25 cases given 100,000 I.U. A.T.S. only 9 recovered, while 1 improved case left against advice. Nineteen out of 37 consecutive cases which received only 20,000 I.U. A.T.S. recovered. The next 15 cases were given only 20,000 I.U. and of these 12 recovered, but other variations on routine treatment invalidate any strict comparison between this and the other groups. We concluded that antitoxin is not the most important single factor in the treatment of established tetanus, but we did make the reservation that in cases with grave prognostic criteria, or where a raw dirty wound may still be a source of exotoxin formation and liberation, a larger dose should perhaps be given. On the other hand, Dr. Herbert Stelling in a personal communication mentions good results using no antitoxin in another mission hospital series in India.

In one respect only do our figures not agree closely with those of Dr. Johnstone. In his series 47 patients died as a direct result of tetanus, though in 2 of these exhaustion and age may have been largely responsible for death. Only 5 cases died of bronchopneumonia and 2 of urinary infection. We concluded from our series that about 66% of deaths were directly related to the spasms, and up to 33% died as the result of superadded infection or exhaustion. These differences may be accounted for as follows:

(*a*) The lower percentage of deaths directly the result of tetanus may have been due to more intensive treatment with sedatives. If spasms cannot be controlled the outlook is serious. Dr. Stelling gave heavy sedation with excellent results in his unpublished series. The danger, of course, is that respiration may be depressed, thus predisposing to chest complications; but these may be prevented in many cases where special nursing can be given.

(*b*) While the higher incidence of secondary infection in our series may have been due to excessive sedation in some cases, it may also have been due to lack of special nursing. Though all possible attention was paid to this aspect of treatment, we were unable, in a small mission hospital with limited facilities and staff, to detail a special nurse to any case of tetanus. Dr. Johnstone was in a more fortunate position in this respect, and the difference in our figures would emphasize the importance of this point. The report of Drs. R. S. Packard, T. B. Cartmill, and J. G. Henry (*Journal*, January 4, p. 16) on the use of large doses of chlorpromazine by continuous infusion, supplemented by intermittent amylobarbitone, which suppressed spasms without depressing respiration, is very encouraging.

Dr. Johnstone states that intragastric intubation was abandoned because the passage of the tube sometimes caused laryngeal spasm. Spraying of the larynx with local anaesthetic will sometimes enable a tube to be passed in difficult cases. However, when the patient will not tolerate a nasal tube, or one cannot be passed, gastrostomy may be of value. It is easily effected under thiopentone, and we have used it recently. In this way fluid and calorie intake may be conveniently maintained, oral hygiene simplified, and the dangers of feeding by mouth reduced.—I am, etc.,

Edinburgh. WILLIAM A. HANNA.

REFERENCE

[1] Hanna, W. A., and Hanna, P. R., *J. Christian med. Ass. India*, 1957, 32, 5.

## Neuropsychiatric Sequelae of Lightning Stroke

SIR,—Dr. James Margerison's mention of focal epilepsy following lightning stroke (*Journal*, December 7, 1957, p. 1370) recalls an interesting case seen in Colombo many years ago. During a monsoon thunderstorm a wayside tree, under which a cow had been sheltering, was struck by lightning just as two men who were sharing an umbrella had reached it. Large splinters of wood flew up into the air "as if from a giant woodcutter's axe." The cow was hurled violently to the ground. The man who was holding the umbrella (in his right hand) collapsed and lay curled up on his side motionless, with his right hand and forearm burned and his shirt sleeve scorched. All this was witnessed by his companion, who had escaped unscathed. With the help of others he revived his friend, who was unconscious, and carried him into a hut near by; he was dazed, trembling, and breathing noisily, but uttered no word. Meanwhile flames had arisen through the rain-sodden crown of the tree and the cow was found to be dead.

The victim of the thunderbolt was referred to me several months later by Dr. G. Amaratunge with an interesting neurological history. For a few days following this mishap the patient had remained dazed, dizzy, and speechless, with stiffness of his neck, twitching, and pins-and-needles sensations in his right upper limb. Under treatment with herbal plasters, decoctions, and inunctions by an Ayurvedhic practitioner, the patient's burns had healed and he had recovered his power of speech and free movement of his neck; but his myoclonic symptoms had persisted and had spread to his right leg. A few months later the case came under the care of my colleague, who had succeeded in controlling the symptoms with bromide and phenobarbitone.

There was no neuropathic history, personal or familial, in this case. The patient was a healthy-looking man in his middle thirties. He had experienced a moderately strong electric shock, several years previously, from a 110-volt A.C. mains circuit, but with no ill effects. He had remunerative employment as a motor mechanic and showed no evidence, past or present, of psychiatric disturbance. He remembered the blinding flash of lightning but nothing else of his mishap as described by his companion. He had experienced a sudden sensation as of having been hit on the root of the right side of the neck with a heavy cudgel—a sensation unlike that felt when he received the electric shock. He was unaware of his burns until he had been revived. Clinical examination revealed no objective signs besides the healed burns. There was no impairment of motor or sensory functions, nor any asymmetry of reflex responses. Retinoscopy was negative. Lumbar puncture was not done. No facilities existed in those days in Ceylon for E.E.G. investigation.

This case would appear to suggest focal cortical disturbance possibly initiated by the effects of electrostatic shock. The patient continued treatment with satisfactory symptomatic relief, and Dr. Amaratunge ceased to hear of him after some months.

During the last war I was asked by the Archdeacon of Colombo to see a teacher in a mission school who had been unsuccessfully treated for epilepsy following a lightning stroke and who was being urged by friends to undergo a "bali" ceremony for exorcism of evil spirits. A radio set that the patient was about to switch off during a thunderstorm had been suddenly hurled from its stand during a flash of lightning without hitting him; but he had experienced a severe shock which had jerked him off his feet *away* from where the radio set had been, while two others at the opposite end of the room felt themselves being drawn *towards* the set. A vivid blue flame had been seen flashing along the copper aerial wire, which was suspended between tall masts opposite the window. The victim of the stroke was picked up trembling with fear, incoherent in speech, and in a state of extreme agitation; he had a burn on his right hand, a gash on his occiput, which had struck the cement floor, and a sprained ankle. He was treated for headache, giddiness, and blurred vision with a sedative mixture by a local doctor. He remained shaky and unsteady for several days and his original symptoms were replaced by insomnia, photophobia, and ataxia. He was apparently cured of these disabilities by Ayurvedhic remedies, but after an interval of good health he developed fits which had persisted.

He presented no history of personal or familial predisposition to fits or nervous disease, but he had over-reacted to an enemy air raid on Colombo on Easter Day, 1943, though he was well outside the danger zone. There was an element of emotional instability in his reactions. His wife, who was a voluble virago and a nursing attendant at a government hospital, seemed to dominate his personality. She answered questions put to him and sharply corrected some of his answers concerning his subjective sensations. He was evidently a mother-fixated individual who was now leaning heavily on his wife as an emotional prop. She recited with much gusto a list of drugs which she had administered to the invalid, the names of which she had obtained

from various doctors under whom she had served, as effective remedies for epilepsy.

Neurological examination revealed no positive findings. There was evidence of guilt feelings associated with the patient's vocational duties, which were revealed on an occasion when he turned up alone for examination. After patient questioning of the man's wife, it became apparent that she had misled the doctors, whose therapeutic advice she had sought, by her insistent diagnosis of "meemasmoray" (major epilepsy) as her husband's malady. This patient's "epileptic fits" were no more than wild, convulsive struggles against those who had to hold him down; they lasted 10 minutes or more at a time, showed no clonic-tonic sequence, nor association with tongue-biting or involuntary micturition. It seemed probable that hyperventilation preceded some of these seizures and that consciousness was not truly lost. Evidently a case of Charcot's "hysterolepsy" had been mistreated as one of true epilepsy. The patient made a satisfactory recovery under pentothal narcosis.

Almost identical symptoms as those of the second case were observed in a man who had inadvertently driven an iron crowbar into a high-tension electric mains cable buried in a spot where he was excavating soil. He received a severe shock and extensive burns, but in view of workmen's compensation advantages he would not co-operate in treatment. —I am, etc.,

Colombo, Ceylon. ERNEST SOYSA.

## Ministry Memorandum on Blindness

SIR,—I should like to comment on the Ministry of Health's *Memorandum on the Prevention and Alleviation of Blindness*, just received by all family doctors, ophthalmic medical practitioners, and opticians in the Health Service. It fails to give a complete list of causes of blindness. It is perhaps understandable that it does not particularly mention diseases of the eye—for instance, retinitis or industrial diseases—apart from injuries, but I feel it should have drawn attention to temporal arteritis. Memoranda, in my opinion, are a waste of time and money if, as in this case, they only enumerate the obvious causes of blindness (with the exception of retrolental fibroplasia) and do not mention a not-so-uncommon condition in old people as temporal arteritis, which has to be diagnosed and treated quickly to achieve success.—I am, etc.,

Epping, Essex. H. KORTE.

SIR,—Having read the small yellow pamphlet entitled *Memorandum on the Prevention and Alleviation of Blindness*, issued and widely distributed by the Ministry of Health recently, I am prompted to make some observations thereon. As an ophthalmic surgeon in a provincial district with a population of about 75,000 I am purely stating my own views on the various items mentioned, in the hope that this may provoke the views of others in the same position as myself.

Dealing with the various paragraphs in their order in the pamphlet, I mention first that I agree that ophthalmia neonatorum and syphilis are almost never seen as causes of blindness in infancy. Retrolental fibroplasia, in spite of having attracted, and quite rightly so, a lot of attention in recent years, is still a very rare disease—at least this appears to be the case in my district. Strabismus raises another interesting point. The inference in the pamphlet is that squint operation will cure the amblyopia ex anopsia which one so often meets in squint cases. This is not so. Adequate orthoptic supervision plus occlusion, as well as surgery, must all be taken into consideration, and even then some cases of amblyopia are intractable from the start and do not improve in spite of treatment.

The remarks on cataract really surprise me. I cannot believe that 80% of people registered blind from cataract have no treatment. There must be other factors present such as proved macula degeneration or retinitis pigmentosa. If this district is anything to judge by I should say that any patient blind from cataract alone would be admitted to hospital within two months of being referred to hospital at the very outside, and this district has notoriously long waiting-lists on account of the small size of its local hospital.

The problem of glaucoma is always a really difficult one: so many patients have vague and disturbing ocular symptoms which very often are psychological. There are few subjects in which the patient's imagination can run away with him so much as that of ocular symptoms. If all these patients were to be referred to hospital for the time-consuming tests which may or may not show up an early glaucoma, then the out-patient departments would be overwhelmed and long waiting-lists for appointments would result. It must be remembered that very often the visual acuity is not affected until the very late stages of the disease, and only accurate perimetry will show up the significant early field losses. Diabetes: in my opinion the control, or lack thereof, of diabetes in its early stages in no way affects the presence or prognosis of diabetic retinopathy.

I have no doubt in my own mind that the increased facilities for registration—and I mean this in the very widest sense—have been the major factors in producing an apparent increase in blindness in this country in the post-war years, and not, as tends to be suggested in the pamphlet, any lack of care by general practitioners or in ophthalmic departments.—I am, etc.,

Peterborough, Northants. G. M. BARLING.

## Bladder Cancer in Chemical Workers

SIR,—Perhaps my friends Professor E. Boyland, Dr. R. A. M. Case, and Mr. D. M. Wallace have been a little hard on the Ministry of Health in their correction of the undoubted error which is quoted in their letter (*Journal*, January 25, p. 222). "Optimistic prolepsis" is not a sin. Had the Ministry simply written "*can be* prevented and eliminated" the correction would not have been necessary but would have opened the way to a reasonable request that, since occupational bladder cancer is not a notifiable disease under the Factories Act, it is or should be incumbent on all practitioners, surgeons, and urologists to obtain as full an occupation history as possible of their cases of bladder tumours and seek guidance as to whether any suspicion of an occupational cause could arise. At present men like Dr. Case can only rely on death data, men like Mr. Wallace on cases he himself meets, and men like Professor Boyland on indications for experimentally testing compounds for carcinogenic properties, which might arise from the occupational history of the dead. What is required is data on the living case and at as early a stage as possible. It is at least possible that other bladder carcinogens than those already detected exist in the complicated ramifications of the organic chemical industry.

At present such data would come fully to light on a living case only if he took an action in common law against his employer on the grounds of negligence in operation of his processes, or if his relatives did so after his death. I need not add that by that time fog descends upon the issue. How much better it would be if workers' organizations, industry, and doctors co-operated openly and without suspicion. It is often a source of considerable disillusion to approach any industrialist for information on the hazards of his products, unless he happens to be a very big or a very exceptional man, and it requires great caution to approach a trade union. Nothing but good can emerge from co-operation, even between donkeys.—I am, etc.,

Chalfont St. Giles, Bucks. M. W. GOLDBLATT.

## Obscure Abdominal Pain

SIR,—Dr. R. T. D. FitzGerald (*Journal*, January 4, p. 42) records the cases of a girl of 14 who "presented with very severe pain in the right iliac fossa with great tenderness and guarding at McBurney's point," in whom an initial diagnosis of appendicular colic was made, and of a man of 30 who complained of pain in the left hypochondrium and was diagnosed and treated as dyspepsia. I find such diagnostic mistakes are surprising.

Pain produced in the appendix, in the stomach, or the rest of the gut is invariably situated centrally in a definite

and constant site for the simple reason that the relative innervation was acquired and the reference map in the cerebrum completed when the gut was a short midline tube. Future migration of certain parts of the later elongated and tortuous intestine alters neither the reference map nor the local sign. The "registered address" remains constant: that is why pain produced in the upper third of the gut is situated in the epigastrium, pain produced in the middle third in the umbilical region, and pain in the colon in the hypogastrium—a simple illusion on the part of the sensorium, which is unaware that certain tissues and organs have been displaced from their early embryonic positions. When pain is experienced in the same *position* as that occupied by the organ at fault we take the coincidence for granted, but when pain is situated at a distance from the tissue in which it is excited (e.g., diaphragmatic pain, testicular pain, etc.) we—or some of us—are tempted to formulate and expound ingenious theories with no embryological or anatomical justification. Hence Mackenzie's viscero-cutaneous reflex, Morley's peritoneo-cutaneous radiation, the irritable focus, etc.—all, in my view, complete myths.—I am, etc.,

Dundee, Scotland. F. R. BROWN.

### "Strive Officiously to Keep Alive"

SIR,—Many of us use the above quotation in support of a plea that it is sometimes unkind to prolong life. It may well be so. Dr. Ian Grant, in his excellent article on the care of the dying (*Journal*, December 28, 1957, p. 1539), appears to use the quotation in this manner. But it is doubtful if the poet meant this.

The particular poem[1] is a mordant and extremely bitter attack on the second-rate attitude to vice and virtue of the Victorians, second-rate in that the main chances were always paramount. For instance, this same poem advises against adultery, but only because there is no profit in it. Any heroic striving by a professional man on his job would, according to the poet, be similarly tempered with the discretion of a good time-server. If I am right the poet meant exactly the opposite to the sense of the words as they stand—as is common in sarcasm.—I am, etc.,

Chester. G. WHITWELL.

REFERENCE

1 Clough, A. H. (1819-1861). "The Latest Decalogue." See *Faber Book of Comic Verse*, 1942, ed. by Michael Roberts. Faber and Faber, London.

### Knock-knee in Children

SIR,—I wonder if any of your correspondents on the above subject (*Journal*, January 4, p. 43) have ever told a mother, "Don't worry, the legs always straighten up spontaneously," and been met with a lift of the skirts revealing well-marked knock knees, the cause of her worry for the child, and the derisive response, "Do they?"—I am, etc.,

Sydney, Australia. C. C. MCKELLAR.

## POINTS FROM LETTERS

**Appendicectomy**

Dr. L. M. SHIRLAW (Romford) writes: If appendectomy means excising the "append" (*Journal*, November 30, 1957, p. 1310), then mastectomy must surely signify removing the "mast."

**Eugenics**

Dr. W. R. E. HARRISON (Buxted, Sussex) writes: People seem to be getting wise to the dangers of applied science in war, but not yet to the dangers of applied science in peace, and not at all as applied to medicine. Yet surely the practice of modern medicine misapplied, or perhaps I should say half-applied, could become more disruptive to the world than atomic bombs. For half a million years treatment has been unavailing, and now quite suddenly we are faced with the fearful responsibility of success. We have abrogated one half of Nature's sanctions; but we are refusing even to contemplate the far harder next step, which must be to devise man-made substitutes at least as good. Yet surely we will be compelled to breed for quality. Surely we will be compelled to put a check on quantity—or go bust. And time, it seems, is not on our side.

# Obituary

## ERNEST JONES, M.D., D.Sc., F.R.C.P.

Dr. Ernest Jones died on February 11 at University College Hospital, aged 79. A collaborator and friend of Sigmund Freud, a scholar, editor, and author of international distinction, and the doyen of British psychoanalysts, he was a revered figure in the world of medical psychology.

Ernest Jones was born at Gowerton, Glamorgan, on January 1, 1879, the son of a mining engineer. From the village school he went on to Swansea Grammar School and then to University College, Cardiff, where he began the study of medicine. He completed his clinical training at University College Hospital, London, where one of his closest friends was Wilfred Trotter, who later married Jones's sister. Qualifying in 1900, he graduated M.B. with first-class honours at London University in the following year, winning gold medals for medicine and obstetrics. He proceeded M.D. in 1903, again winning a gold medal, took the M.R.C.P. in 1904 and the D.P.H. of Cambridge in 1905. After qualification he held a long series of hospital appointments: he was house-surgeon, house-physician, and senior obstetric assistant at U.C.H.; clinical assistant at the National Hospital, Queen Square, the Hospital for Sick Children, and the Royal London Ophthalmic Hospital; registrar and pathologist at the West End Hospital for Nervous Diseases; senior physician at the Farringdon Dispensary; assistant physician at the Seamen's Hospital; and lecturer in practical neurology at the London School of Clinical Medicine. His early interest was neurology, and he began to contribute to *Brain* within a few years of graduation. A period of postgraduate study at Munich helped him to master the German language, and, an avid reader, he eagerly seized on the copious writings of German neurologists and psychiatrists. In particular he was profoundly impressed by Freud's studies and himself began to use psycho-analysis in his work, describing his results in the *Journal of Abnormal Psychology* in 1909. He went to Vienna, met Jung and Freud, and heard the latter speak at the first International Congress of Psycho-analysis; from then on he was a confirmed Freudian.

[*Camera Press, Ltd*

In 1908 Jones went to Toronto as demonstrator of medicine and psychiatry at the university, and as psychiatrist at the Toronto General Hospital. Later he was appointed professor of psychiatry at Toronto. Shortly before the first world war he returned to England, having first revisited Freud and his collaborators in Vienna. For the rest of his life he was to work in London, being soon recognized as the leading psycho-analyst in the English-speaking world. The founder and president of the British Analytical Society and of the Institute of Psycho-analysis, he later became president of the International Psycho-analytical Association. He was also director of the London Clinic for Psycho-analysis and editor of the *International Journal of Psycho-analysis* from its foundation in 1920 until 1939.

At the time of the invasion of Austria by the Nazis Freud was 82 and too old and tired to move from Vienna on his own initiative. But Ernest Jones flew out to Vienna and succeeded in bringing back Freud and his family to London, where they were able to settle down in peace. Freud died in 1939.

Ernest Jones was the author of many papers and monographs and of several books. His *Papers on Psycho-analysis* reached its fifth edition in 1948. During the last few years he had been occupied on his biography of Freud—*Sigmund Freud, Life and Work*—the three volumes of which were welcomed throughout the world as a work of major importance and lasting value. Several of his papers were published in this *Journal*; and in 1956, in celebration of the centenary of the birth of Freud, he contributed a special article on "Freud and his Achievements." We also published his address on "The Nature of Genius" which he read at the Royal Society of Medicine in the same year.

A formidable adversary, Ernest Jones was a stout defender of psycho-analysis in many controversies. He served on the Psycho-analysis Committee of the B.M.A., and its report, published in 1929, contained Ernest Jones's own answers to the criticisms which had been advanced against the theory and practice of psycho-analysis. The committee expressed no collective opinion, but agreed that "the term 'psycho-analysis' can legitimately be applied only to the method evolved by Freud and to the theories derived from the use of this method." Elected F.R.C.P. in 1942, Jones was awarded the honorary degree of D.Sc. by the University of Wales in 1954—a distinction which gave him particular pleasure. In 1944, when he gave up the active presidency of the British Psycho-analytical Society, the Ernest Jones Lectures were founded to commemorate his work.

Ernest Jones's intellectual energy and ability to apply himself to the problems in hand were quite exceptional. It was qualities of a similar kind which made him a leading figure-skater. He began skating seriously only in his forties, but he did not give up the sport until he had written an authoritative work on the subject entitled *The Elements of Figure Skating*. In later years he enjoyed playing chess with his friends.

Ernest Jones was twice married. His second wife, Katherine Jokl, whom he married in 1919, survives him together with two sons and a daughter.

We are indebted to Dr. EDWARD GLOVER for the following appreciation: The death of Ernest Jones removes from the scene one of whom it may be said with justice that he left his mark on his times. For Dr. Jones was not only a distinguished physician and the sponsor of psycho-analysis in English-speaking countries, he was a man of outstanding cultural attainments whose trenchant personality and writings exerted an influence on modern humanism that deserves to be recorded *magna cum laude*. As his earlier academic and professional record indicated, he would assuredly have gained distinction in any branch of medicine he chose to pursue: but a happy chance brought him early in his career in contact with the work and person of Freud. From then until the day of his death Ernest Jones threw himself wholeheartedly into the task of advancing and spreading the teachings of his Homeric mentor. When it is recalled that during that early period the adherents of psycho-analysis could be counted almost on the fingers of two hands and that those pioneers had to fight their way through dense thickets of prejudice to gain breathing space and a platform for the new ideas, the magnitude and arduousness of their task may become apparent to a modern generation which, whether or not it agrees with the principles and practices of psycho-analysis, has come either to accept or to reckon with it as a firmly founded and internationally recognized branch of science.

Dr. Jones was singularly well qualified to throw down the gauntlet for an unpopular scientific cause. Intellectually he had what might be described as a commando training, and combined this mental equipment with that singular tenacity of purpose and pugnacity of spirit which thrives on opposition. Keen and nimble of wit, immensely industrious, an encyclopaedic reader with an unusually retentive memory for significant detail, scrupulously erudite, with a translator's grasp of the German tongue (in which all that was then worth while in psycho-analysis was written), a lucid exponent of difficult ideas, an accurate, polished, and on occasion persuasive writer, a formidable controversialist with a sharp tongue and an infallible nose for a weak argument, Ernest Jones soon took a leading part in the development of psycho-analysis, first in the U.S.A. and, on his return from Canada, in London, where he set up the original London Psycho-analytical Society. At first the full weight of representing and defending psycho-analysis in this country fell on his shoulders, and he was constantly involved in the many controversies that raged in psychological societies and congresses towards the end of the first world war and for some years afterwards. Many of his contemporaries can still recall with relish the memorable exchanges that took place between the giants of the time—McDougall, Rivers, Shand, Burt, Spearman, Hart, Flugel, Baynes, and many others. In this distinguished gallery Jones rapidly acquired the reputation of being a formidable opponent, to be treated with wholesome respect and an equally challenging proponent to be listened to with close attention.

As this gladiatorial phase gradually passed the fruits of his more unobtrusive administrative labours for psycho-analysis came to light and are now recorded in the history of the British Psycho-analytical Society, the *International Journal of Psycho-analysis*, the *International Psycho-analytical Library*, the London Clinic of Psycho-analysis, and the Institute of Psycho-analysis, all of which he founded, directed, or, as the case may be, edited, and nursed with devoted skill until they were able to stand unaided on their own feet. His work for the International Psycho-analytical Association was equally lengthy and productive. He was a founder member of this association, on numerous occasions acted with distinction as its president, and when he finally retired was appointed with acclamation its permanent honorary president.

But these achievements as an organizer, administrator, teacher, translator, editor, advocate, and entrepreneur, brilliant though they were, do not constitute Jones's sole claims to distinction. More significant in this respect was his work as a research student in clinical psycho-analysis and in those branches of applied analysis which bring the psycho-analyst in close contact with man's cultural activities and aspirations. Jones was a voluminous writer of whom it could be said that whatever he wrote was worth reading, either by professional colleagues and students or by those interested in what the psycho-analyst would call the cultural sublimations of man's primitive instincts. To be sure, a large proportion of his published work was inevitably didactic. Indeed, for many years his *Papers on Psycho-analysis* was, after Freud's *Introductory Lectures*, the nearest to a textbook of psycho-analysis extant in English. His essays on dreams, on symbolism, and his outline of psycho-analytical theory were models of erudite yet entirely lucid exposition. His clinical essays, though not so imaginative or creative as those of his master Freud, broke ground in many directions and were invariably characterized by thoroughness, a logical application of principles, and accurate documentation. An early monograph on character formation and anal-erotism remains to this day the definitive work on the subject. Indeed, there were few clinical aspects of psycho-analysis to which Jones did not contribute useful and informative papers, as witness his studies of suggestion, anxiety, hate, jealousy, and other root problems in medical psychology.

It was, however, through his work on applied psycho-analysis that Jones came to acquire a wider reputation and to add to the lasting literature of humanism. And it was characteristic of him that he never contributed to, for example, anthropology, folklore, sociology, or linguistics without first versing himself thoroughly in the principles and methodology of the cognate science he was invading. Similarly with his work on literature and the arts. His essay on *Hamlet* was a model of the applied method, and his psycho-analytical exposé of this subject has been accorded the recognition of quotation by his most thorough-paced

opponents among Shakespearian critics. During the last years of his life in retirement Ernest Jones laid the copestone on this reputation by producing his monumental biography of Freud, a labour of love to which he applied the whole armament of his talents and which will stand as a permanent work of reference alike to psycho-analytical students, biographers, and scholars of all degrees.

To attempt to convey in a few sentences what manner of man was Ernest Jones is to court almost certain failure. Having literally devoted his life, in and out of season, to psycho-analysis, it was inevitable that he should in course of time "introject his object," to use the cant analytical phrase; in other words, that the lineaments of his character should come to personify his all-consuming interest. There were not many who were accorded the privilege of passing this professional barrier; nor, even to intimates, were there many occasions when he would lower his cultural visor. Behind this protective façade he was a fascinating mixture of simplicity and complexity. Simple in tastes, and, though capable of intense feeling, simple in temperament; endowed with a sensitiveness that sharpened his naturally quick perceptions, but which at times verged almost on touchiness and made him impatient of wits duller than his own; readily aroused to a smothered wrath yet possessed of a light, ironic, salty humour that played around the foibles of mankind; a confirmed realist who was nevertheless capable of simple, sentimental accesses (after all, he was a Welshman born and bred, and such illusions as he fostered were in the romantical and classless tradition of the Principality); in moments of relaxation an engaging and always a vivacious companion, Ernest Jones achieved easily the ambition of being distinguished also in his private life. His character and personality constituted indeed his greatest creative achievement, and there can be few who met him during his later years who will readily forget that aquiline and ascetic face that bore on it the distinguishing marks of deep experience, met, as was his death, with a fortitude that bordered on stoicism.

MRS. JOAN RIVIERE writes: The achievement of Ernest Jones in his life-work of introducing and establishing the psycho-analytic discoveries of Freud in this and many other English-speaking countires marks him out as in certain ways a quite exceptional personality. Weighty opposition confronted his efforts, especially in early days before the first world war, and no one but himself was equal to shouldering the task. The few supporters he had were not of the same calibre. Apart from the high degree of intellectual ability he possessed, in which, though outstanding, he was not of course unique, it would seem that what enabled him to achieve this objective was the outcome of two special features in his character. The first is the most important and the most rare. It consists in an acute faculty of perception, of insight—a propensity to recognize evidences of intrinsic worth and value when and where they appear, and to respond with a sure instinct of affirmation to that recognition. The strength and persistence of this trait in him were the mainspring of his work; it dominated him and outweighed those inhibitions which cause most of us to overlook or lose touch with various good things that are accessible. This capacity to recognize value was by no means limited to his appreciation of the work of Freud; it played an important part in his role as a leader, enabling him to utilize elements in different people of many different, even conflicting, kinds, in order to serve the main purpose in view. It was also evidently the source of another characteristic—the wide range of his interests.

The other feature of his personality formed the main instrument by which his success was achieved—namely, his outstanding capacity to take action. Undismayed by obstacles, he would apply every energy and every available means to further the ultimate aim—that of, in the long run, promoting and establishing the new knowledge; alternatively, any objective of the moment which would assist that aim. Whatever was needed must be done and would be done: in his early years opposition and difficulties of all kinds may even have stimulated his efforts. His courage and his persistence were unshakable. These qualities were evident, whether in the long course of his life's work or in an immediate emergency, such as his response to the sudden danger to Freud in the Nazi invasion of Austria—a story in which his powers of courage, resourcefulness, and unremitting energy are vividly illustrated.

## W. R. P. GOODWIN, D.S.O., M.R.C.S.

Colonel W. R. P. Goodwin, formerly Assistant Director-General of the Army Medical Services, died on January 30, aged 82.

William Richard Power Goodwin was born on May 26, 1875. He came of a family closely linked to medicine and to the Army: his father was Surgeon Major John Goodwin, who joined the Army in 1855, and his eldest brother, Lieutenant-General Sir John Goodwin, was Director-General of the Army Medical Services from 1918 to 1923. From Newton College, Devon, W. R. P. Goodwin went on to St. Mary's Hospital to study medicine, and joined the R.A.M.C. in 1900, the year in which he qualified. For some years he was in India, where he served as personal assistant to the Principal Medical Officer, Punjab Command. Thereafter he was medical officer at the Royal Arsenal, Woolwich, for three years. In 1910 he returned to India and was serving there at the outbreak of the first world war. He left with the first Indian contingent for France, serving in that theatre throughout the war, being awarded the D.S.O. and being promoted brevet colonel at the conclusion. For a few months after the Armistice Colonel Goodwin was commandant of the Michelam Convalescent Home for Officers, Mentone, returning to England in the spring of 1919 to take up the appointment of senior medical officer at the Royal Military College, Sandhurst. In 1923 he took command of the Military Hospital, Gibraltar. From 1926 to 1929 he was Assistant Director-General of Army Medical Services at the War Office, and his last appointment before his retirement in 1932 was that of A.D.M.S., East Anglian Area. From 1928 to 1932 he was Honorary Physician to the King.

The year after he retired Colonel Goodwin became medical officer to Eastbourne College, and he worked in that capacity until 1947, except during the second world war, when he was in charge of the Red Cross and St. John Officers' and Convalescent Hospital at Somerley, Ringwood.

Colonel Goodwin married Myrtle, youngest daughter of the late Elton Forrest, in 1907, and she survives him with three sons, Commodore D. G. Goodwin, Naval Attaché at Washington, Major-General R. E. Goodwin, now a divisional commander, and Dr. J. F. Goodwin, a physician on the staff of the Hammersmith Hospital.

W. P. MacA. writes: Colonel Goodwin's death will revive many affectionate memories among his large circle of friends. Persons who were not very shrewd judges of others might at first have failed to recognize the fine character that lay behind a modest and unassuming bearing; but, as such an acquaintanceship progressed, so would the appreciation of his qualities rise in proportion. And it is always pleasing to meet people who do not have all their goods displayed to the first inquiring glance. Colonel Goodwin aimed at a high standard of performance on his own part, and his example and counsel were an inspiration to all who served under his command. Apart from his skill in his special subject of ophthalmology, he had a wide and sound knowledge of medicine, and a visiting consultant when faced with

some difficult problem in diagnosis might well profit from Colonel Goodwin's experience and saving common sense. He was particularly anxious that members of other branches of the Service should realize what has been achieved by preventive medicine since the days when it was expected that more fighting men would perish from epidemics of war—like the spotted fever and the bloody flux—than from all other diseases and all enemy assaults put together; so when possible he used to arrange for a series of garrison lectures on subjects of this kind which lend themselves to making a story at once informative and interesting to the lay mind.

One characteristic of both Colonel and Mrs. Goodwin that left its mark wherever they were stationed was an open-handed and untiring hospitality in which all ranks shared; and they held that entertaining of this nature was the plain duty of every officer so far as his particular circumstances allowed. Our sympathy goes out to Mrs. Goodwin and to her three sons.

## DAVID THOMAS, M.D.

Dr. David Thomas, of Tollcross, Lanarkshire, died on November 26, 1957, in his 91st year. He was in active practice until a year before his death, and even at his great age was loath to retire.

David Thomas, a son of the manse, was born at Lockerbie, Dumfriesshire, on September 9, 1867. Educated at George Watson's College and at Edinburgh University, he graduated M.B., C.M. in 1893, proceeding to the M.D. five years later. His first experience of practice was as an assistant to Dr. Thomson, of Darlington, and in 1896 he returned to Scotland as assistant to Dr. Willis at Baillieston, Lanarkshire, one of whose daughters became his wife about two years later. After marriage he set up in practice in the neighbouring villages of Tollcross, Carmyle, and Mount Vernon and practised there for the next fifty-seven years.

R. A. L. writes: It is difficult to pay adequate tribute to that fine and lovable old man David Thomas. His was a day and generation which has virtually passed into oblivion, to the great loss to medicine. The family doctor of his day was more than the family physician, and many of his patients revered him for his kindly advice and sympathy in smoothing out their personal problems and difficulties. He upheld the highest traditions of medicine, and with his kindliness and skill soon attracted an extensive practice. His patients loved him, and his popularity and worth were recognized in 1954, when a social evening was arranged in his honour and he was presented with a handsome gift of books. Among his other attributes he was widely read and a most erudite scholar deeply versed in the classics. Literature was his great joy, and as he was a purist in grammar he did not take kindly to modern usage of certain words and phrases, many of foreign origin, which he regarded as slovenly and ungrammatical.

Dr. Thomas was a deeply religious man, but owing to the calls of practice felt he could not devote adequate time to church work and therefore regretfully refused eldership. Happy in his home and marriage, he suffered grievous loss with the death of his wife, though he accepted the blow with commendable fortitude. He is survived by his son, with whom he was in partnership, and two married daughters. With his death there passes one of the old family doctors who personified all that was fine in medicine.

## DOROTHY K. PATERSON, M.B., D.P.H.

Dr. Dorothy Paterson, school medical officer and assistant medical officer to the Southend-on-Sea county borough, died at her home at Thorpe Bay on January 9 after a short illness. She was 43 years of age.

Dorothy Kirby Paterson, a niece of the late Dr. E. H. Walker, formerly medical officer of health for Stretford, Lancashire, was born on August 20, 1914. From the Ilford County Girls' High School she obtained scholarships to the Royal Free Hospital for Women, qualifying M.R.C.S., L.R.C.P. in 1939. In the same year she graduated M.B., B.S. from London University. After qualification she held appointments at Queen Mary's Hospital, Carshalton, and at several London hospitals during the second world war. In 1948 she became school medical officer and assistant medical officer to the county borough of Southend-on-Sea, an appointment she held until her untimely death. She took the D.P.H. of the English Royal Colleges in 1949.

J. S. L. writes: Dr. Dorothy Paterson's duties were mainly connected with schools and schoolchildren, but she was also medical officer to the Southend council's residential institutions for children and medical officer to the infant welfare centre, additional appointments which gave her further scope. Her association with the nursery and children's homes was probably the most completely satisfying of all her professional activities, but her concern for the children went beyond their medical care, for she came to know some of them very well, and she interested her friends in the activities of the homes. To a wide clinical experience and excellent judgment there was added an instinctive and sympathetic understanding of children, who quickly gave her their trust. As a colleague she was always helpful, self-effacing, and utterly reliable. Some years ago her health began to give anxiety, and she received a warning that boded no good for the future. She bore illness with quiet fortitude, exemplary patience, and considerable self-discipline, co-operating to the full with her advisers. On her return to duty she made no mention of her ordeal, and asked for no concessions. In recent months her friends had noted with pleasure some lessening of her shy reserve and an enhancement of her natural serenity. Her death has come as a painful shock to all who knew her, and her colleagues and the children in Sea View Homes will miss her greatly. Her affection and solicitude for her mother, with whom she lived, were unobtrusive but deep, and our profound sympathy goes out to Mrs. Paterson in her bitter loss.

## NORMAN BRODIE, M.R.C.S., L.R.C.P.

Dr. Norman Brodie, who was a general practitioner in Blackpool, died there on January 12. He was 53 years of age.

Norman Brodie was born at Capetown on May 5, 1904, and was educated in South Africa. He came to Britain to study medicine and began his clinical work at the London and Charing Cross hospitals. He suffered a grievous blow by the death of his parents, and as a result had to give up the study of medicine. He later became a medical representative with a London drug house. In 1942 he joined the R.A.M.C. as a private, and, while stationed at York, was permitted by the Army authorities to recommence his medical studies. He qualified in 1945 at the age of 41 and was at once commissioned. He later spent three years in B.A.O.R. as a deputy director of medical services, being demobilized in 1948 with the rank of major. His home was now in Blackpool, where he entered general practice after working as casualty officer and clinical assistant at the Victoria Hospital.

R. A. F. writes: Dr. Brodie was possessed of a most affable manner and was very patient by disposition. He instilled confidence into all who came under his care, and was a pleasant and likable colleague. A sudden cardiac episode in 1955 left its inevitable mark, and though he continued to work until the day before his admission to hospital in March, 1957, he was in a precarious state of health. His death was peaceful, and the severe trials and tribulations of the previous ten months were cheerfully and courageously borne. He leaves a widow, a son, Dr. Norman Harry Brodie, who has just completed his term of National Service as a surgeon lieutenant in the Royal Navy, and a daughter, to all of whom we extend our deepest sympathy.

## REX STANSFELD, *M.C.*, B.Chir.

Dr. Rex Stansfeld, who formerly practised at Hailsham, Sussex, died at his home at East Preston, in the same county, on January 28. He was 69 years of age.

Rex Stansfeld, who was born on July 2, 1888, was a man with many interests and diverse abilities. His upbringing was in the narrow Victorian tradition, and the main relaxation encouraged in his home was music. For this he showed much aptitude, and, having an accurate ear and a remarkable voice, he sang at the Temple Church and a solo at the coronation of King Edward VII. Having won a choral scholarship to St. John's College, Cambridge, he became a medical student and obtained first-class honours in the Natural Sciences Tripos. Going on to St. Bartholomew's Hospital for his clinical training, he qualified in 1913 and completed a resident appointment at about the time the first world war broke out. Thereupon he joined a hospital ship transporting wounded across the Channel. While on this work he met Mabel Fairbrother, a nursing sister, and they were married in 1915. After joining a small practice at Hailsham in East Sussex, Stansfeld very soon volunteered again and became medical officer to the Scots Rifles Brigade in the 52nd Division, with which he served, first in Palestine and then in France, where he was awarded the Military Cross for gallantry and distinguished service in the field. After the war he returned to Hailsham. There, over the years, he built up a large practice, looking after the local maternity and isolation hospitals as well as being police surgeon and workhouse medical officer. He was chairman of the Eastbourne Division of the B.M.A. in 1934–5. In spite of a busy practice he found time to pursue his hobby of model ship building and to take up Freemasonry enthusiastically. He applied to his models the principles of naval architecture used in the construction of full-sized ships, and, although he showed his work at a few exhibitions, he derived his main pleasure from demonstrating them to his friends and patients. As a Freemason he was particularly interested in the academic side of the craft, and he amassed one of the foremost collections of books on Freemasonry in the country.

In retirement he was as busy as ever. For most of the last twelve years of his life he lived alone, his first wife having died in 1938 and his second wife dying only two years after their marriage. He took a delight in building up a garden of rare shrubs; he continued his model-making and Freemasonry; he built up a collection of glasses; he re-read the classics; and he found time to be a genial host. He was a short cheerful man who could discuss almost any subject intelligently. He died from a bronchial carcinoma, and, although well aware of the nature of his last illness, he accepted it calmly, speaking of it without causing any embarrassment. He retained a sense of humour to the end, so that his numerous visitors enjoyed going to see him.

## A. STEPHEN NIVEN, M.D.

Dr. A. Stephen Niven died at his home at South Croydon on February 7 at the age of 78. He had been in general practice in Thornton Heath for very nearly 40 years.

Adam Stephen Niven was born on December 6, 1879, and was educated at Aberdeen University, where he graduated M.B., Ch.B. in 1903, proceeding to the M.D. five years later. Soon after graduation he settled in practice in his native Aberdeenshire, first at Rothie-Norman, where he stayed only a year or two, and then at Turriff. There, in addition to his practice, he became medical officer to the Turriff and District Fever Hospital and to the Turriff, Auchterless, and Forglen parishes. Later he became also medical officer to the Post Office and a certifying factory surgeon. In 1919 he moved south to enter general practice at Thornton Heath, in Surrey, and was thus actively engaged until early last year.

H. F. H. writes: We shall miss Dr. Adam Stephen Niven very much in Croydon. His sunny, humorous, Aberdeen temperament brought a welcome breath from the north, where he always returned for holidays. He well illustrated the saying that only reliable sound men ever come from Aberdeen University. He first practised near home, and then, in 1919, came to Thornton Heath, where he spent the rest of his professional life. I first met him during the second world war at the medical boards, where his pawky Scottish humour and keen common sense were an ever-present help and joy. His colleagues and patients became his friends, and he was an ideal general practitioner. His interest in and knowledge of antiques were exceptional. His wife died recently, and he himself was severely crippled for many months, but he never allowed his disability to alter his temperament. He leaves a son, now a colonel in the R.A.M.C., and a daughter to carry on the fine tradition.

## N. D. MATSON, F.R.C.S.Ed., D.L.O.

Mr. N. D. Matson, consulting ear, nose, and throat surgeon to the Mid-Glamorgan group of hospitals, died at his home at Cadoxton, Neath, on February 1. He was 55 years of age.

Neill David Matson was a New Zealander by birth, but was always proud to recall that he was also of Scottish descent. Educated at Canterbury University College, Christchurch, and at Otago University, he came to London to study medicine at Charing Cross Hospital, qualifying in 1929. After holding the appointment of house-surgeon at the Coventry and Warwickshire Hospital, he returned to New Zealand, where he was house-surgeon at the Christchurch Hospital for a time. He came back to England and took the D.L.O. of the English Royal Colleges in 1931, and was appointed senior house-surgeon at the Birmingham Ear and Throat Hospital. For the next few years he held other hospital appointments at Walsall, Birmingham, and Hull. After serving with the Merchant Navy in the Pacific during the war, he again returned to Britain to become resident surgeon at Queen Mary's Hospital, Roehampton, and in 1948 he took the F.R.C.S.Ed. Some two years later he was appointed consulting ear, nose, and throat surgeon to the Mid-Glamorgan group of hospitals. He will be remembered by his colleagues as a man who, although handicapped in recent years by failing health and severe pain, always upheld the high tradition of his profession. The sincere sympathy of all who knew him goes out to his widow and three young children, the eldest being only 6 years old.

## J. C. BRASH, *M.C.*, M.D., F.R.C.S.Ed., D.Sc. LL.D., F.R.S.Ed.

Dr. J. R. A. TODHUNTER writes: May I be allowed to add a personal tribute to the memory of Professor James Couper Brash, whose obituary appeared in your issue of January 25 (p. 223)? I was first associated with him in the 10th Field Ambulance on the Somme in 1916, and some five years later we both found ourselves situated in Birmingham, and for the past thirty-five years I was privileged to enjoy his close friendship. He was a man who would have made his mark in whatever profession he had adopted, for he possessed a keen and active mind, and in all he did, whether work or play, he pursued it with zest. And these abilities were leavened by a lively sense of humour, which made him a delightful host and companion. We had known that his health was rather precarious for several months past, but hoped that he would be able to continue moderate activity for some time to come. In a letter written only nine days before his death he said he was improving and was busy on the proofs of the revision of *Cunningham's Manual of Practical Anatomy*. He was eagerly looking forward to the arrival home on leave in April of his daughter, who is a medical missionary in India, but that reunion, alas,

was not to be. To her and to his son, who is an administrative officer of British Railways at Edinburgh, our sympathy goes out, as well as to his wife, who made his home life a happy one for forty-five years and the basis of his achievements.

### W. J. HOPE-ROBERTSON, M.B., F.R.C.S.Ed. F.R.A.C.S., D.O.M.S., D.L.O.

The obituary of Mr. W. J. Hope-Robertson was printed in the *Journal* of January 25 (p. 228).

A colleague in New Zealand writes: Walter Hope-Robertson decided early to take up eye, ear, nose, and throat surgery, and embarked on a most comprehensive postgraduate career in England. He held clinical assistantships at Moorfields and at the Central London Ophthalmic Hospital. In addition, he was on the staff of the Wolverhampton and Midland Counties Eye Infirmary and the Birmingham Ear, Nose, and Throat Hospital. In 1928 he returned to New Zealand and began practice in Wellington. For the last twenty years he confined himself to ophthalmology.

From 1929 till his death Walter Hope-Robertson played a prominent part in the work of the Wellington Hospital. He was active in the reorganization of the specialist departments of the hospital and later controlled an expanding and highly successful ophthalmological department. For many years before his death he represented the visiting staff in its associations with the hospital board, and he was chairman of the medical staff of the Wellington Hospital. An outstanding feature of his professional life was his contact with ophthalmologists in other parts of the world. He was instrumental in bringing many distinguished ophthalmic surgeons to New Zealand. He was a major force in founding the Ophthalmological Society of New Zealand, a body of which he was secretary-treasurer for ten years and president in 1956.

Walter Hope-Robertson held the highest place in New Zealand medicine by reason of his special skill, knowledge, and integrity. He had a forward-looking mind, eager to capitalize on advances in his sphere, and a nature never satisfied with anything but the best. Early in life he suffered a rheumatic infection with involvement of the heart. This disability, which was responsible for his death, did not prevent his leading a full life, carried on fearlessly and with a full knowledge of the implications of his cardiac disability. In his private life he was notably kindly and thoughtful and in the happy atmosphere of his home exercised his love of literature, with a particular interest in the Maori history of New Zealand.

### GWYNNE WILLIAMS, M.D., M.S., F.R.C.S.

The obituary of Mr. Gwynne Williams was printed in last week's *Journal* (p. 403).

A. J. G. writes: May I be allowed to record a personal note of appreciation about my old chief, Mr. Gwynne Williams? I worked under him as a dresser and later as surgical registrar, and later still it was my privilege to be his colleague. When I was his dresser just after the first world war there was little formal teaching, and the student had perforce to build up most of his factual knowledge from his own clinical observation and from the textbooks available. This left many gaps, and I have always been grateful to Gwynne Williams for showing me at this stage how shrewd common sense could fill them in. To be a successful "Bill Dresser" in those days implied a capacity for hard work and a readiness to take hard knocks. In turn we were rewarded by an occasional shy aside which was enough to show us that the great man did not really feel himself so much above us.

The amount of work which went on in the early days was tremendous, and Gwynne Williams spared neither himself, his house-surgeon, nor his dressers in his determination to see that all was well for his patients. His standards remained the same throughout the years. Common sense came first, science was regarded with a certain amount of suspicion, and the interests of the individual patient were never allowed to suffer.

Those who met Gwynne Williams only occasionally often carried away with them an impression of a man with fixed ideas, unbending, unforgiving, and unable to make allowances. In fact he was too shy to make contact very readily with a colleague or with an examination candidate, and too conscientious to give way when he thought he was right; but in spite of this he was a very shrewd and kindly judge of people and their abilities. When he discovered his reputation as a harsh examiner he was desperately hurt, and perhaps this made him even more retiring in his latter years. He contributed to the surgical side at U.C.H. a tradition of hard work and unfailing honesty coupled with a deep distaste for personal aggrandizement, and we are very grateful to him.

## Medico-Legal

### DOCTOR IN ACTION OVER PATIENT'S WILL

[FROM OUR LEGAL CORRESPONDENT]

In 1952 Miss Madeleine Zarro, who had come to England early in the century, was left some £20,000 by a Mr. Ashman, to whom she had been nurse during his last illness. After this she did not change her mode of living, which had always been modest.

That October a Dr. J. J. Golding was called to attend her at her home. He thought she was very ill and wanted her to go to hospital, but she refused to go either to hospital or to a nursing-home, and Dr. Golding undertook to treat her at home. She rapidly improved and by the following March was much better, but when Dr. Golding suggested that his visits might cease she objected, and he continued to visit her.

Miss Zarro became friendly with her doctor, and in the spring of 1954 told him she wanted to leave him shares in a building society. Though he discouraged her Miss Zarro was insistent, and talked him into agreeing to be an executor if she would find a second person to act. She next asked him to recommend her to his solicitors. Dr. Golding gave her the names of four solicitors in four different firms. She selected a Mr. Gerald Williams, and gave him instructions for a will, which was executed on June 24, 1954. Miss Zarro told Mr. Williams that she had no family and would like him to share with Dr. Golding the residue of her estate after various legacies, including one to the doctor of £5,000 worth of building society shares, about which she gave precise instructions. Mr. Williams also tried to discourage her and get her to take other advice, but she insisted, and the will was drawn accordingly.

In November, 1954, Miss Zarro suffered as a result of a street accident a cerebral injury from which she never recovered, and she died on March 28, 1955. Dr. Golding therefore was entitled under the will to £5,000 worth of building society shares and about £5,000 as half the residuary estate.

Both Dr. Golding and Mr. Williams, faced with the embarrassing situation of the professional man whose client insists on leaving him a large sum of money, had acted with discretion and propriety. This did not prevent them from becoming the target, in a probate action[1] brought by a lady who would have been a legatee under a former will of Miss Zarro, of allegations of undue influence. It was said that Miss Zarro at the time the will was executed was not of sound mind, memory, and understanding, and was unable to understand the nature of the testamentary act. It was

[1] *The Times*, February 4, 5, and 7.

alleged that Dr. Golding and Mr. Williams had procured the making of the will by undue influence. After the mid-day adjournment on the third day of the hearing before Mr. Justice Willmer, and after Dr. Golding and other witnesses had given evidence and been cross-examined, the action was settled and the allegations of undue influence against Dr. Golding and Mr. Williams were withdrawn.

This case shows how important it is for any doctor whose patient tells him he intends to leave him a large sum of money to insist on the patient having completely independent advice. Doing so did not save Dr. Golding from an action, but at least it ensured that, although he was subjected to the unpleasantness and expense of fighting, he emerged with his honour untarnished.

## SUDDEN DEATH IN PRISON FROM FULMINATING INFLUENZA

At 6 a.m. on Christmas Day, five weeks after committal to H.M. Prison, Barlinnie, Glasgow, J. B., a prisoner aged 24, was summoned from his cell for "slopping out," along with other prisoners in the same hall. When one of the two prison officers on duty unlocked his cell J. B. appeared all right. He said nothing to the officer. He carried his basin and chamber to the toilet, a distance of about 15 yards (13.7 m.), emptied them, and returned to his cell and made his bed. Half an hour later, when the two prison officers were re-locking the prisoners in their cells, they heard J. B. shouting "Screw!"* in a strange voice, and they saw him standing at the door of his cell. By the time they reached the cell, however, he had collapsed on his bed. He was lying on his back with his arms across his stomach and his eyes were rolling. He was sweating profusely, but conscious, saying repeatedly, "Do something for me," "Don't leave me." The prison officers sent for a nursing officer at once, but J. B. died within ten minutes of first calling for help.

At the inquiry into his death, held at the Sheriff Summary Court, Glasgow, on December 30, Dr. D. A. R. Anderson, the prison medical officer, testified that he had last seen J. B. alive on December 21, when he had reported sick, complaining of a cold. Little wrong was found with him then except for a raised pulse, but he was sent to bed for the day. Dr. Robert Greenhill, the assistant medical officer, said he saw J. B. on December 22 and again on December 23. He had no fever and on the second day said he was much better and asked to return to work. However, as his pulse was still up, Dr. Greenhill marked him for employment in his cell for the next few days. Dr. Anderson, in his evidence, added that at the request of the police he had looked at two abrasions on the deceased's face, but they had been caused two or three days before death.

The post-mortem examination was carried out by Dr. D. Bruce Neilson and Dr. Edgar Rentoul at 11.15 a.m. on December 26. They found some mucoparulent material in the trachea, and a large amount of blood-stained frothy fluid in the bronchi and bronchioles. Both lungs were markedly congested and oedematous, with extensive and widespread areas of haemorrhage. There was no upper respiratory obstruction. The heart was not enlarged, but there were a few petechiae on the anterior surface of the left ventricle, and the muscle was pale and flabby. The abdominal organs were congested, the kidneys and supra-renals intensely so, and the spleen was slightly enlarged and soft. The brain was very congested and the grey matter was "of a somewhat violet hue." There was no evidence of any cranial injury. Dr. Neilson and Dr. Rentoul formed the opinion that J. B. died from a fulminating influenzal bronchopneumonia. The Sheriff, after considering the evidence, found that J. B.'s death was due to this cause.

Four other cases of fatal fulminating influenza seen in Glasgow by Dr. Neilson are reported elsewhere in this issue (p. 420).

*Prison slang for a prison officer.

# Medical Notes in Parliament

## HEALTH SERVICE CONTRIBUTIONS

Mr. D. HEATHCOAT AMORY, Chancellor of the Exchequer, in a statement to the House of Commons on February 18 disclosed that the total net estimates for 1957–8 would amount to £4,260m. Increasing cost over the years on the Health Service had caused the Government particular concern. When the Service was constituted the gross cost was expected to be £175m., and the share borne by the Exchequer £126m. This expectation was immediately falsified and the cost had risen greatly from the start. Next financial year the gross cost was estimated at £740m. On present arrangements the Exchequer's share would be £555m. This was over four times as large in money terms and nearly three times in real terms as was originally contemplated, and represented a higher proportion of the total than was envisaged at the outset of the Service. The Government had decided that the whole of this vastly increased charge could not be borne by the Exchequer. Accordingly they proposed that with effect from the beginning of July next the National Health Service contribution—which was a separate contribution collected with the insurance stamp—should be increased. The increase would be 6d. for men, 4d. for women, and 2d. for juveniles, with in each case an additional 2d. from the employer. The additional yield from these increased contributions would be about £24m. next year and £32m. in a full year. On this basis the individual (and his employer) would still only be paying a stamp or charges for just under 20% of the gross cost of the Service—that being the figure it was originally proposed that he should bear.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) called attention to the national drugs bill, which amounted to £50m. a year, in great part due to expensive proprietary drugs, and asked that it should be examined before the Goverment went further with this increase. She also asked whether this meant that there was to be no increase in the prescription charge and no charge for treatment at a doctor's surgery, as had been forecast in a certain Sunday newspaper. Mr. HEATHCOAT AMORY said the Minister of Health was keeping a very close check on the Health Service expenditure. They could have cut standards or cut service or increased the charges. They decided on this occasion that the right thing to do would be that the extra burden should be carried by the fit rather than by those in trouble. The answer to the last question was, "The present proposal is as I have described it." The Chancellor also said in a further reply, "At present we have no proposal for increasing the charges."

## DOMICILIARY CARE FOR THE AGED

In reply to an adjournment debate on February 12 on the welfare of old people, initiated by Mr. ANTHONY KERSHAW (Stroud, Con.), Mr. RICHARD THOMPSON, Parliamentary Secretary, Ministry of Health, ran over the health and welfare services which are available to them at home. A local health authority was required to provide a service of health visitors to give advice on the care of persons suffering from illness and on the care of others. The total number of visits by general duty health service visitors in 1956 was about 11 million, and it was estimated that about 1 million of the visits were to the aged and chronic sick. The health visitor's advice on diet, hygiene, and general care could, of course, be of the greatest value to the elderly and to those living with them and helping with their care. The next important aid was the home nursing section. Under Section 25 of the National Health Service Act, 1946, local health authorities were required to provide a service of nursing to those needing it in their own homes. There had been encouraging growth here, and there was no doubt that it had met an increasing need on the part of the aged sick who might otherwise have had to go into hospital. The

number of nurses employed had risen from 7,758 at December 31, 1948, to 10,104 at December 31, 1956, and during a roughly comparable period the number of patients attended had risen from 865,000 to 1,097,000. These cases had involved more than 24,652,000 visits, of which more than half were to patients who were aged 65 or over at the time of the first visit during the year, and the increasing proportion of the demand by the aged was shown by the fact that only three years earlier, in 1953, the proportion of the cases in respect of those aged 65 and over attended was one-third of the total number.

The next important contributory service was home helps. They undoubtedly did a remarkable job. All local health authorities had made provision for such a service, and it was being increasingly used for old people who through a few hours' help each week might be enabled to continue to live in their homes. Old people often needed such help for an indefinite period, but the extent of the help given might be limited—indeed, it was often—by the pressure of other demands on the service, some of which—maternity cases, for instance—must be given priority. The number of home helps employed had increased from 11,338 at December 31, 1948, to 39,056 at December 31, 1956. Sixty-eight per cent. of the applications for home help so provided during 1956 were from households needing help because of the presence of somebody who was elderly or was chronically sick. He would like to dwell in some detail upon the other services which contributed to this conception of care for elderly people in their own homes, but he could not do very much more than mention them simply by name. There was the night attendance and evening service; the laundry service, which was a useful one, because laundry created great problems for many elderly people, especially the bedridden and incontinent; and the "meals on wheels" service. In most areas this was provided by voluntary agencies, usually with a subsidy from the local authority, and it was doing a very fine job. Then there was a chiropody service, provided by a small number of local authorities and a large number of voluntary organizations either at clinics of their own or in conjunction with old people's clubs.

### Antidote to Radiation Poisoning

Sir WAVELL WAKEFIELD (St. Marylebone, Con.) asked the Minister of Health on February 11, in view of the progress in the United States with research into the possibility of producing a drug to counteract poisoning or death by radiation in the event of a nuclear war or accident, what advance had been made in the United Kingdom in this direction. Mr. D. WALKER-SMITH stated that the Medical Research Council had for some ten years actively supported work on substances that might protect against the effect of ionizing radiations. Substantial progress had been made experimentally, but the results were not yet applicable to the treatment of human beings.

### Influenza Vaccine

Mr. S. P. VIANT (Willesden, West, Lab.) asked the Minister of Health on February 12 how much influenza vaccine was bought officially from the United States of America in 1957. Mr. WALKER-SMITH: None.

### Paralytic Poliomyelitis

Mr. S. P. VIANT asked how many cases of paralytic poliomyelitis were recorded during 1957; how many of them recovered; and how many were under 15 years of age. Mr. WALKER-SMITH stated that the provisional figure for notifications of paralytic poliomyelitis in 1957 was 3,172. The other information was not available exactly in the form requested. Up to June 30 the provisional number of deaths assigned to acute poliomyelitis was 52, and out of 2,497 cases of paralytic poliomyelitis notified up to September 30, 1,650 were children under 15.

### Merit Awards

The Minister of Health informed Dr. DONALD JOHNSON (Carlisle, Con.) that the total number of merit awards paid to consultants in England and Wales at December 31, 1957, was 2,343, at a total annual cost of about £2m., equivalent to approximately 25% of the estimated total of the recipients' salaries, including the awards.

### New Metropolitan Hospital Board

Mr. JOHN MORRISON (Salisbury, Con.) asked the Minister on February 13 whether he could announce his decision on the proposal to set up a separate regional board for the western area of the South-West Metropolitan Hospital Region.

Mr. WALKER-SMITH replied that consultation of the bodies concerned had shown that the great majority of opinion supported the proposal of the South-West Metropolitan Regional Hospital Board for a separate hospital region and board for this area, and he had decided to accept it in principle. But in the present financial circumstances he did not consider it justifiable to incur the additional costs of administration which would inevitably be involved in the creation of a new board, and he was therefore deferring action until a more appropriate time.

### Ventricular Septal Defects

Mr. RICHARD THOMPSON informed Mrs. JOYCE BUTLER (Wood Green, Lab.) on February 10 that equipment for the surgical closure of ventricular septal defects in young children was available or would shortly become available at the following centres: Shotley Bridge General Hospital, Consett; Leeds General Infirmary; City General Hospital, Sheffield; Papworth Hospital, near Cambridge; Hammersmith Hospital; Middlesex Hospital; St. Bartholomew's Hospital; Guy's Hospital; Radcliffe Infirmary, Oxford; Bristol Royal Infirmary; Sully Hospital, near Cardiff; Queen Elizabeth Hospital, Birmingham; Royal Liverpool Children's Hospital; Broadgreen Hospital, Liverpool; and Sefton General Hospital, Liverpool. Later Mr. Thompson told Mrs. Butler, in reply to another question, that the operation was still at an early stage of development and it was not yet possible to say when or whether it would be performed at all these centres.

### Coal-gas Poisoning

Sir FRANK MEDLICOTT (Central Norfolk, Ind. Con.) asked the Paymaster-General on February 17 if, in view of the large number of people who were accidentally killed every year through escaping gas, he would set up an inquiry into the possibility and desirability of gas being given a pungent and, if practicable, an acrid smell which would penetrate to an extent sufficient to awaken persons from sleep.

Sir IAN HOROBIN, Parliamentary Secretary, Ministry of Power, said the Gas Council had been carrying out experiments to test the effects of adding odorants to town gas. But it was doubtful whether a smell, however pungent, would awaken persons from sleep, and the British Medical Association did not recommend the addition of irritants to the gas in order to achieve this purpose. He added in other replies that the number of fatal accidents had risen from 552 in 1950 to 934 in 1955, with a reduction to 865 in 1956. An analysis of records maintained by the Gas Council showed that, of the accidental deaths in 1956, approximately 80% were caused by the misuse of appliances, 10% by faulty domestic apparatus, and 7% were due to causes outside the consumers' control. There were a number that could not be classified.

---

*Chiropody Service.*—The Minister of Health informed Mr. E. L. MALLALIEU (Brigg, Lab.) on February 17 that the estimated cost of providing a free chiropody service would be rather more than £1,250,000 a year.

*Transistor Hearing-aids.*—It is hoped to begin providing transistor hearing-aids for children within two or three months. The aids will not be available for adults until next year.

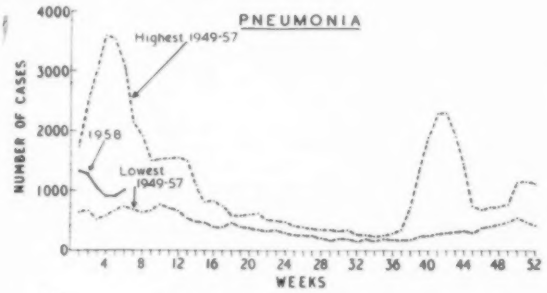
# Vital Statistics

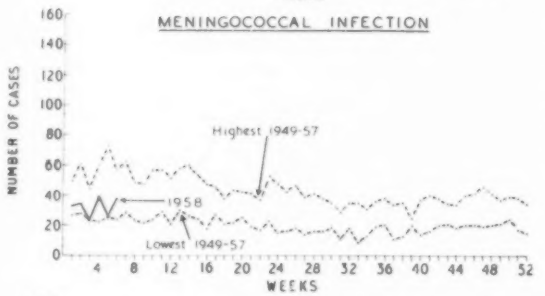
### England and Wales Weekly Returns Changed

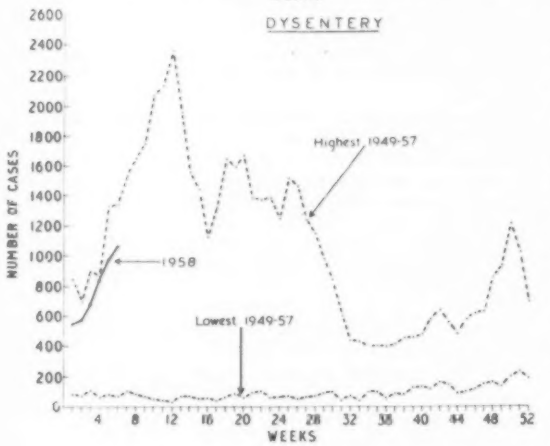
The weekly totals of births and deaths in England and Wales are now recorded from the whole country and not from the 160 great towns. The Registrar-General has introduced this change from the week ending February 1 (No. 5). In consequence no comparable figures of births and deaths for 1957 can be recorded in our Table of Infectious Diseases and Vital Statistics, and the graph comparing weekly numbers of deaths from influenza with those of previous years will not be published for the time being.

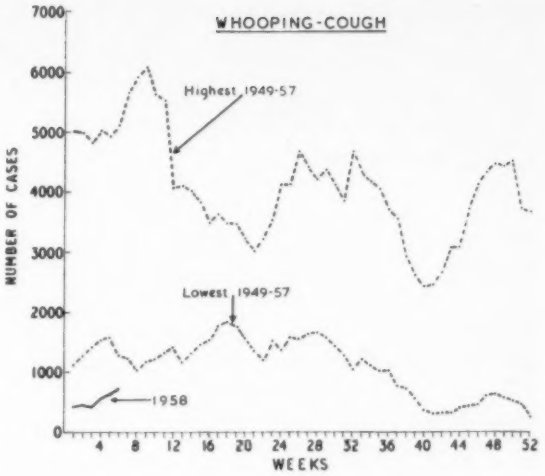
### Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus - - - - - -, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.




### Week Ending February 8

The largest increases in the notifications of infectious diseases in England and Wales during the week ending February 8 were 279 for measles, from 3,473 to 3,752, 114 for acute pneumonia, from 909 to 1,023, 96 for dysentery, from 964 to 1,060, and 76 for whooping-cough, from 645 to 721; no large decreases in incidence were reported. Deaths from influenza in the 160 great towns numbered 75, and were 22 fewer than in the previous week. The weekly totals of influenza deaths have decreased for the last four weeks.

The largest rises in the incidence of measles were 88 in Glamorganshire, from 350 to 438 (Swansea C.B. 239); 58 in Southampton county, from 220 to 278 (Havant and Waterloo U.D. 86, Portsmouth C.B. 68); 45 in Buckinghamshire, from 52 to 97 (Chesham U.D. 42); 42 in Kent, from 87 to 129 (Sheerness U.D. 55); the only large fall was 60 in Montgomeryshire, from 71 to 11. The notifications of scarlet fever numbered 871, being 9 fewer than in the preceding week, and there were no large fluctuations in the local returns. The largest variations in the trends of whooping-cough were a rise of 30 in Somersetshire, from 30 to 60 (Bridgwater M.B. 24), and a fall of 28 in Warwickshire, from 71 to 43. 3 cases of diphtheria were notified, being 1 more than in the preceding week; 2 of the cases were notified in Birmingham C.B. The largest increase in the returns for acute pneumonia was 40 in London, from 80 to 123.

The notifications of acute poliomyelitis numbered 20, and these were 12 more for paralytic and 3 fewer for non-paralytic cases than in the preceding week. The largest returns were Southampton county 4 (Winchester M.B. 2, Basingstoke R.D. 2) and Lancashire 3 (Liverpool C.B. 2).

The largest rises in the outbreaks of dysentery were 45 in London, 35 in Yorkshire West Riding, and 28 in Cambridgeshire; the largest fall was 31 in Durham. The chief centres of infection during the week were Lancashire 331 (Oldham C.B. 86, Middleton M.B. 40, Liverpool C.B. 33, Chadderton U.D. 24, Manchester C.B. 22, St. Helens C.B. 21, Whiston R.D. 11, Bolton C.B. 10, Royton U.D. 10), London 182 (Finsbury 45, Islington 39, Stoke Newington 22, Fulham 17, Bethnal Green 13, Southwark 13), Yorkshire West Riding 179 (Sheffield C.B. 59, Saddleworth U.D. 35, Huddersfield C.B. 15), Cambridgeshire 52 (Cambridge M.B. 29, Cheston R.D. 23), Caernarvonshire 33 (Bangor M.B. 32), Yorkshire North Riding 33 (Middlesbrough C.B. 24), Durham 24, Middlesex 22, Staffordshire 20 (Newcastle under Lyme M.B. 11), and Cheshire 20.

## INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 1** (No. 5) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

| CASES | 1958 | | | | | 1957 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire |
| Diphtheria | 2 | 0 | 4 | 0 | 1 | 5 | 0 | 2 | 0 | 5 |
| Dysentery | 964 | 137 | 159 | 8 | 3 | 1,097 | 80 | 195 | 6 | 1 |
| Encephalitis, acute | 3 | 0 | | 0 | | 2 | 0 | | 0 | |
| Enteric fever: | | | | | | | | | | |
| Typhoid | 2 | 0 | 1 | 0 | | 3 | 0 | 0 | 0 | 3 |
| Paratyphoid | 4 | 0 | 1(B) | 0 | 5(B) | 10 | 1 | 0 | 0 | |
| Food-poisoning | 145 | 14 | 51 | 0 | | 181 | 38 | 35 | 1 | |
| Infective enteritis or diarrhoea under 2 years | | | | 5 | 25 | | | | 10 | 24 |
| Measles * | 3,473 | 56 | 77 | 41 | 12 | 13,008 | 971 | 494 | 451 | 316 |
| Meningococcal infection | 26 | 4 | 14 | 1 | | 32 | 1 | 15 | 0 | |
| Ophthalmia neonatorum | 27 | 1 | 1 | 0 | | 21 | 1 | 2 | 0 | |
| Pneumonia † | 909 | 80 | 356 | 19 | 8 | 661 | 41 | 300 | 15 | 4 |
| Poliomyelitis, acute: | | | | | | | | | | |
| Paralytic | 4 | 1 | 1 | 1 | 1 | 28 | 3 | 7 | 1 | 4 |
| Non-paralytic | 7 | 1 | | | | 9 | 1 | | | |
| Puerperal fever § | 239 | 41 | 6 | 0 | | 234 | 47 | 11 | 0 | |
| Scarlet fever | 880 | 56 | 80 | 22 | 19 | 865 | 77 | 83 | 34 | 22 |
| Tuberculosis: | | | | | | | | | | |
| Respiratory | 619 | 69 | 133 | 16 | | 631 | 73 | 124 | 14 | |
| Non-respiratory | 63 | 3 | 23 | 6 | | 87 | 7 | 14 | 4 | |
| Whooping-cough | 645 | 41 | 35 | 7 | 11 | 3,302 | 173 | 502 | 19 | 67 |

| DEATHS | 1958 | | | | | 1957 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire |
| Diphtheria | 0 | 0 | 0 | 0 | 0 | No comparable figures available. | 0 | 0 | 0 | 1 |
| Dysentery | 3 | 0 | | 0 | | | 0 | | 0 | |
| Encephalitis, acute | | 0 | | | 0 | | 0 | | | 0 |
| Enteric fever | 1 | 0 | 0 | 0 | | | 0 | 0 | 0 | |
| Infective enteritis or diarrhoea under 2 years | 15 | 0 | 0 | 0 | 2 | | 1 | 2 | 0 | 1 |
| Influenza | 204 | 15 | 3 | 0 | 1 | | 0 | 1 | 1 | 1 |
| Measles | | 0 | 0 | 0 | 0 | | 1 | 1 | 0 | 1 |
| Meningococcal infection | | 0 | 0 | | | | 0 | 1 | | |
| Pneumonia | 1,086 | 81 | 40 | 37 | 20 | | 60 | 23 | 15 | 7 |
| Poliomyelitis, acute | 3 | 0 | | 0 | 0 | | 0 | | | 0 |
| Scarlet fever | | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Tuberculosis: | | | | | | | | | | |
| Respiratory | 115 | 6 | 17 | 3 | 5 | | 7 | 14 | 4 | 1 |
| Non-respiratory | | 0 | 1 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Whooping-cough | 1 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Deaths 0–1 year | 427 | 32 | 39 | 10 | 19 | | 38 | 38 | 8 | 8 |
| Deaths (excluding stillbirths) | 14,138 | 1104 | 809 | 199 | 237 | | 828 | 692 | 147 | 171 |
| LIVE BIRTHS | 14,704 | 1203 | 1083 | 235 | 392 | | 1167 | 1003 | 181 | 446 |
| STILLBIRTHS | 330 | 37 | 24 | | | | 31 | 25 | | |

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

# Medical News

**Annual Dinner of the Hunterian Society.**—At the annual dinner of the Hunterian Society, held at the Savoy Hotel on February 13, the medical profession had its collective leg briskly pulled by two judges. Sir GERALD UPJOHN, proposing the main toast, translated the Latin motto on the Society's crest, *Ratio Societatis Vinculum*, as "Good-O, we've got a stranglehold on the people generally." He said that the Hunterian Society would be doing a very great service to the medical profession if it used its influence to reduce the amount of committee work overburdened doctors were called upon to do: it was appalling that doctors had to spend so much time attending committee meetings of all kinds. Speaking of the Society's president, Mr. J. C. Ainsworth-Davis, Sir Gerald said that he belonged to a specialty whose members might suitably be described as "hewers of stone and drawers of water." In reply Mr. AINSWORTH-DAVIS gave an account of the year's activities. The strength of the Society was still growing, the membership having gone up from 306 ten years ago to 461 in 1958. The attendance at the dinner was a record. Sir WALTER FERGUSSON HANNAY proposed the health of Sir DENIS TRUSCOTT, the Lord Mayor of London, who, in reply, appropriately described the jewels in his badge of office as "very large stones of the finest water." The health of the guests was proposed by Lord EVANS. After welcoming the presidents of the Royal Colleges, he said that they were sorry that Dr. Ian Grant, president of the College of General Practitioners, could not be present because of indisposition, but were very glad to see Dr. G. I. Watson in his place. If British medicine was to thrive, or even survive, under the new order, it must all depend on that sound physician, the family doctor. This view was held, said Lord Evans, by most of the people in high places in medicine. Replying for the guests, Sir MELFORD STEVENSON gave what he called a "terminal injection" with a needle as well barbed as any from the bottom of a doctor's bag.

**British Drug Exports.**—British exports of drugs and medicines reached a new record in 1957 of £39.6m., compared with £35.9m. in 1956 and £12.8m. in 1946. In 1957 antibiotics accounted for nearly £9m.; miscellaneous proprietary medicines accounted for nearly £11m. and vitamins for over £3m. More than 780 million aspirin tablets were exported. Synthetic antimalarials, alkaloids, barbiturates, insulin, and sulphonamides also made important contributions to the total. The leading markets were Australia (£3.4m.) and India (£2.9m.), and New Zealand, South Africa, Nigeria, the Irish Republic, and Burma all took drugs worth £1–£2m. Exports to China also exceeded £1m., an increase of over £300,000 on the previous year. Recent gains in North America were consolidated, exports to Canada and U.S.A. amounting to over £1.5m. Exports to Egypt, however, in view of the political situation, amounted to only £83,000, compared with £1.2m. in 1955 and £740,000 in 1956.

**Medical Advisers to Pharmaceutical Industry.**—An association of medical advisers to the pharmaceutical industry was formed last October. Professional topics of common interest will be discussed at the three or four meetings to be held each year. The first post-inaugural meeting was held at the Royal Society of Medicine on January 23. This was followed by a dinner. The secretary of the association is Dr. E. V. B. MORTON, Newcastle Court, Newcastle Circus, Nottingham.

**Films of "The Hurt Mind."**—The Ministry of Health has informed local authorities that 16 mm. sound films have been made of four of the "telerecorded" programmes in the B.B.C.'s television series "The Hurt Mind." The films can be hired from the Central Film Library, Government Building, Bromyard Avenue, Acton, London, W.3. The titles, running times, number of reels, and hiring charges

(plus 1s. for each extra day per reel) are: *Part 1*, "Put Away," 46 minutes, 5 reels, 25s.; *Part 2*, "Break-down," 29 minutes, 3 reels, 15s.; *Part 3*, "Psychological Treatment," 30 minutes, 3 reels, 15s.; and *Part 4*, "Physical Treatment," 33 minutes, 3 reels, 15s. The Ministry hopes that local authorities will be able to use Parts 1, 3, and 4 "to further the spread of the more enlightened attitude towards mental illness which the T.V. programmes did so much to foster." Part 2 is recommended for more specialized teaching purposes.

**"Journal of Bone and Joint Surgery."**—The British half of this combined Anglo-American periodical has now been in existence for ten years, an event that was celebrated at a small party last week, when Sir WALTER MERCER, on behalf of the editorial committee, presented a silver salver to the editor, Sir REGINALD WATSON-JONES. The journal is published by Messrs. E. and S. Livingstone of Edinburgh, and tribute was paid on this occasion to Mr. CHARLES MACMILLAN for the part his firm had played in the journal's success.

**Welfare of Spastics.**—The medical advisory committees of the British Council for the Welfare of Spastics and the National Spastics Society met at the Hospital for Sick Children, Great Ormond Street, last month, under the chairmanship of Professor A. A. MONCRIEFF. Professor Moncrieff is chairman of the National Spastics Society's medical advisory committee. After discussion of subjects of mutual interest it was agreed to hold a further joint meeting of the full medical committees in six months' time, and thereafter, it is hoped, twice yearly. This is regarded as a first step towards closer integration of the work of the two societies, at least at professional and technical level.

**Accidents in the Home.**—The MINISTER OF HEALTH has asked local authorities and hospitals to co-operate in a drive to reduce accidents in the home, particularly burns and scalds. According to a pamphlet accompanying the request, of the 6,000 fatal home accidents in England and Wales each year about 700 are due to burns and scalds, and "in spite of the publicity given to this subject during recent years the position has not improved." Children under 5 and the aged are the chief victims. Clothes catching alight accounts for about 80% of the deaths.

**Swiney Prize for Medical Jurisprudence.**—The council of the Royal Society of Arts announces that the next Swiney prize will be awarded in January, 1959. The prize, consisting of a valuable cup and £100 in cash, is awarded every five years to the author of the best published work on, alternately, medical or general jurisprudence. On the coming occasion the prize will be for medical jurisprudence. The last date for entries—or for recommendations for works to be considered by the judges—is November 30. Entries or recommendations should be addressed to the secretary, Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2.

**London University.**—Dr. M. L. THOMSON, senior lecturer at the London School of Hygiene and Tropical Medicine, has been appointed to the university readership in applied physiology tenable at the School. Dr. GEORGE BROWNLEE, D.Sc., of King's College, and Dr. MILES WEATHERALL, of the London Hospital Medical College, have had conferred on them the title of professor of pharmacology; and Dr. W. ROBSON, D.Sc., of King's College, that of professor of biochemistry. Dr. H. HARRIS, of the London Hospital Medical College, receives the title of reader in biochemical genetics; Dr. B. E. D. COOKE, of Guy's Hospital Medical School, the title of reader in dental medicine; and Dr. J. P. QUILLIAM, of St. Bartholomew's Hospital, the title of reader in pharmacology.

**Phenoxymethylpenicillin Tablets.**—The 1958 *British Pharmacopoeia* will give a dosage of 125 to 250 mg. for phenoxymethylpenicillin tablets, it is understood, and will require 125 mg. tablets to be dispensed where the prescriber has not specified a strength. The new *B.P.* comes into force on September 1. The 1957 *British National Formulary*, however, requires a tablet of 120 mg. to be dispensed in the absence of specific directions by the physician. Pharmacists hold appreciable stocks of 120, 125, 240, and 250 mg. tablets of phenoxymethylpenicillin. To resolve the difficulty, until further notice the 120 and the 125 mg. tablets, and the 240 and 250 mg. tablets, are made interchangeable when prescribed on Form E.C.10. This applies to proprietary as well as to official preparations.

**Eli Lilly Fellowship (South Africa).**—Applications are invited from medical practitioners registered in South Africa for the 1958 Eli Lilly medical research Fellowship (South Africa). The Fellowship is for the purpose of medical research and is not intended for postgraduate clinical study. The net value is 300 dollars a month for 12 months, plus return travelling expenses to the point of study in the United States of America. Further details can be obtained from Dr. H. A. SHAPIRO, P.O. Box 1010, Johannesburg. The closing date for application is April 30.

**Abraham Colles Lecture.**—The fourth Abraham Colles postgraduate lecture was delivered at the Royal College of Surgeons in Ireland on February 10 by Dr. O. THERON CLAGETT, of the Mayo Clinic. He reviewed the surgery of cancer of the breast.

**Liverpool University.**—Dr. C. A. CLARKE, lecturer in clinical medicine, has been appointed to a readership in the department of medicine.

**W.H.O.**—Dr. CONSTANTIN VINOKOUROFF, of the Neurological Institute of the U.S.S.R. Academy of Medical Sciences, has been appointed director of the World Health Organization's division of therapeutic substances.

## COMING EVENTS

**French Films.**—French scientific and medical films, February 26, 8.15 p.m. at the Institut Français du Royaume-Uni. Tickets from the Scientific Office, French Embassy, 22, Wilton Crescent, London, S.W.1.

**Ciba Foundation Lecture.**—Professor DANIEL BOVET, of Rome, will deliver the tenth annual Ciba Foundation lecture on March 5 at 5 p.m. at Manson House, 26, Portland Place, London, W.1. His subject will be "The Experimental Basis of Neuroleptic and Tranquillizing Therapy." Admission by ticket (free) from the Ciba Foundation, 41, Portland Place, London, W.1.

**Hospital Sterilization Procedures.**—Conference sponsored by the Sheffield Regional Hospital Board at Nottingham University, April 2. Details from the secretary to the Board, Fulwood House, Old Fulwood Road, Sheffield, 10.

**Backward Children.**—National conference of the Guild of Teachers of Backward Children, April 18 and 19, at Goldsmith's College, New Cross, London, S.E.14. Further details from Mr. S. S. SEGAL, 10, Fielding House, Boundary Road, London, N.W.8.

**C.M.F./M.E.F. Physicians' Reunion Dinner.**—April 26, at Simpson's-in-the-Strand. Details from Dr. A. WILLCOX, 59, Harley Street, W.1.

**Hugh Cairns Memorial Lecture.**—Sir GEOFFREY JEFFERSON, F.R.S., will deliver the first Hugh Cairns memorial lecture of the Society of British Neurological Surgeons on March 14 at 5 p.m. at the London Hospital. His lecture is entitled "Sir Hugh Cairns." Tickets are obtainable from Mr. D. W. C. NORTHFIELD, F.R.C.S., The London Hospital, Whitechapel, London, E.1.

**Hospital Equipment and Medical Services.**—The First International Hospital Equipment and Medical Services Exhibition, sponsored by the Institute of Hospital Administrators, will be held at Olympia, May 5–10. The Minister of Health has agreed to open the exhibition.

## NEW ISSUES

### SPECIALIST JOURNALS AND ABSTRACTS

*The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.*

**British Journal of Industrial Medicine.**—Issued quarterly (£3 annually). The new issue, Vol. 15, No. 1, includes:

THE TREATMENT OF EXPERIMENTAL SILICOSIS WITH COMPOUND 48/80. J. Marks, Dinah M. James, and T. G. Morris.
IMMUNOLOGICAL FACTORS IN THE PATHOGENESIS OF THE HYALINE TISSUE OF SILICOSIS. E. C. Vigliani and B. Pernis.
TOXIC PROPERTIES OF SOME DIALKYL AND TRIALKYL TIN SALTS. J. M. Barnes and H. B. Stoner.
PULMONARY DISEASE AMONGST SISAL WORKERS. Hugh Scott.
HEAT STRESS IN NON-FERROUS FOUNDRIES. D. Turner.
SOME CLINICAL AND ADMINISTRATIVE ASPECTS OF OCCUPATIONAL HEALTH. Kenneth P. Duncan.
DERMATOSES IN THE MANUFACTURE OF GLASS FIBRE. William B. McKenna, J. F. Ferguson Smith, and Donald A. Maclean.
ABSENCE FROM WORK IN RELATION TO WAGE LEVEL AND FAMILY RESPONSIBILITY. R. D. Shepherd and J. Walker.
STUDIES ON THE RISKS ASSOCIATED WITH THE USE OF PARATHION-IMPREGNATED GAUZE STRIPS IN FLY CONTROL. Jon Glömme and Å. Swensson.

**British Journal of Ophthalmology.**—Issued monthly (£6 annually). The new issue, Vol. 42, No. 2, includes:

VASCULARIZATION OF THE PRIMARY OPTIC PATHWAYS. J. François, A. Neetens, and J. M. Collette.
CAPILLARY-GLIA RELATIONSHIPS IN THE HUMAN OPTIC NERVE, CHIASMA, AND TRACT, AS SHOWN BY PHASE-COLOUR CONTRAST AND MICRODISSECTION. C. A. Erskine.
OPTIC DISC OEDEMA IN THE ABSENCE OF RAISED INTRACRANIAL PRESSURE. M. J. Roper-Hall.
NON-PIGMENTED INTRA-EPITHELIAL MELANOMA OF CORNEA. P. B. Schofield.
BLOOD SUPPLY OF THE OPTIC NERVES AND CHIASMA AND ITS CLINICAL SIGNIFICANCE. Brodie Hughes.

**Abstracts of World Medicine.**—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

## SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

### Monday, February 24

GUY'S HOSPITAL.—5 p.m., Endocrine Demonstration. Sex Inversion. Guest speaker, Dr. P. E. Polani.
MANCHESTER MEDICAL SOCIETY: (1) SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 5 p.m., Professor K. Bullock: "Xylocaine" (Lignocaine) and Other Local Anaesthetics. (2) SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University, 9 p.m., Dr. M. T. Parker: Uses of a Bacteriological Laboratory to General Practitioners.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. E. Lawson McDonald: Aspects of the Assessment for Cardiac Surgery.

### Tuesday, February 25

B.B.C. TELEVISION.—9.30 p.m., "Your Life in Their Hands." No. 3—A New Lease of Life, from the Queen Elizabeth Hospital, Birmingham.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor C. H. Stuart-Harris: Adenoviruses and Respiratory Disease in Man.
FOUNTAIN HOSPITAL.—5.30 p.m., subject: Deafness and Mental Deficiency. Papers by Dr. L. Fisch: Differential Diagnosis of Deafness and Mental Deficiency; Miss Mary Evans: Rehabilitation.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. B. Russell: Tuberculosis of the Skin.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor H. Bertha (Austria): Brain Tumour and Cerebral Circulation.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. R. Sampson Handley: Carcinoma of the Breast.
ROYAL STATISTICAL SOCIETY: MEDICAL SECTION.—At Westminster Medical School, S.W., 5.30 p.m., Mr. S. Rosenbaum: Pulheems.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Mr. A. J. Wrigley: Postmaturity.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. J. Minton: Ocular Manifestations in Clinical Neurology (Part II).

### Wednesday, February 26

BRITISH ASSOCIATION OF SPORT AND MEDICINE.—At St. George's Hospital Medical School, 5.45 p.m., Mr. Harold Abrahams: The Photo-finish; Mr. W. E. Tucker: Treatment of Sports Injuries.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Recent Advances in the Study of Ringworm Infections.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. T. Holmes Sellors: Surgery of Atrial Septal Defects.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. A. R. C. Higham: Kidney Neoplasms.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor J. H. Dible: Pathology of Lower Limb Ischaemia.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Burns Lecture by Dr. Jan Brod (Prague): Some Haemodynamic Aspects of Hypertension in Relation to the Pathogenesis of the Disease.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE: EDINBURGH BRANCH.—At Edinburgh Royal Infirmary, 5 p.m., Dr. George M. Edington: Malignant Disease in Africa, with Special Reference to Cirrhosis and Hepatic Carcinoma.
SOCIETY FOR ANALYTICAL CHEMISTRY.—At Royal Society, Burlington House, W., 4.30 p.m., annual general meeting. 5 p.m., Bernard Dyer Memorial Lecture by Sir Hugh Linstead, M.P.: Science and Politics.

### Thursday, February 27

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor G. W. A. Dick: Poliomyelitis.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. F. Borrie: Nodular Conditions of the Legs.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., joint meeting with Medical Women's Federation. Miss Isabel'a Forshall: Some Affections of the Genital Tract in the Female Child.
ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Physiology Department, Queen's College, Small's Wynd, Dundee, 5 p.m., Dr. W. W. Park: Significance of Sex Chromatin.
UNIVERSITY COLLEGE LONDON.—At Anatomy Theatre, Gower Street, W.C., 1.15 p.m., Dr. D. W. James: Wounds and Scars in Skin.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, Gower Street, W.C., 5 p.m., public lecture by Dr. F. H. C. Crick: Nucleic Acids—(3) Speculation and Prospects.

### Friday, February 28

BRITISH TUBERCULOSIS ASSOCIATION.—At 26, Portland Place, W., 4.30 p.m., meeting in co-operation with Metropolitan Regional Thoracic Societies. Dr. P. R. Evans and Mr. C. A. Keogh: The Chesty Child. Discussion to be opened by Dr. J. C. Roberts and Dr. E. G. Sita-Lumsden.
● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. B. Dowling: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Mr. W. McKenzie: Clinical demonstration.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in pathology by Sir Howard Florey, F.R.S.: Reaction of the Arterial Wall to Injury.
PLYMOUTH MEDICAL SOCIETY.—At Freedom Fields, 8.30 p.m., Sir Cecil Wakeley, Bt.: Some Aspects of Malignant Disease.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 10 a.m., Mr. David Levi: Abdominal Pain in Children. (2) 4 p.m., Dr. J. F. Goodwin: Peripheral Vascular Disease.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., Mr. J. J. C. Cormack: The Society's Library.
ROYAL SOCIETY OF HEALTH.—At Town Hall, Oxford, 10.15 a.m., Mr. J. C. Riddell: Modern Methods of Sewage Treatment; Dr. G. F. Willson: Asthma in Schoolchildren.

### Sunday, March 2

NORTHAMPTON MEDICAL SOCIETY.—At Northampton General Hospital, 8 for 8.30 p.m., Dr. Donald Hunter: Exploring the Dangerous Trades.

## APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—J. S. Comaish, M.B., Ch.B., Medical Registrar, Ipswich and East Suffolk Hospital; K. C. Basappa, M.B., B.S., Orthopaedic Registrar, King's Lynn Hospital Group; Jean L. Baker, M.B., Ch.B., D.Obst.R.C.O.G., and B. N. M. Ariffin, M.B., B.S., Registrars in Obstetrics and Gynaecology, Norfolk and Norwich Hospital Group; J. Graham Ross, B.M., B.Ch., J. M. S. Haeue, M.B., B.S., and J. C. Simpson, M.D., Surgical Registrars, Ipswich and East Suffolk Hospital; J. Hood, M.B., Ch.B., Medical Registrar, Newmarket General Hospital; G. S. Joss, M.B., Ch.B., Registrar in Plastic Surgery, Regional Plastic Surgery and Burns Unit, West Norwich Hospital; I. G. Tait, M.B., B.Chir., D.C.H., Registrar in Chest Medicine, Ipswich Chest Clinic, and St. Helen's Hospital, Ipswich; D. G. A. Westbury, M.B., B.S., Registrar in Psychiatry, Suffolk Mental Hospitals.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Appleton.**—On January 25, 1958, to Pearl (formerly Osborn-Smith), wife of Norman Appleton, F.R.C.S., of 89, Queen's Road, Oldham, Lancs, a third son—Christopher.
**Chambers.**—On February 8, 1958, to Barbara June, wife of Douglas Robert Chambers, M.B., B.S., a brother for Barbara Lynn—Robert Mark.
**Davis.**—On January 31, 1958, to Margaret (formerly Liddle), S.R.N., wife of Leslie R. Davis, M.D., of 9, Forrest Gardens, Norbury, S.W., a daughter—Julia Margaret.

### DEATHS

**Bingham.**—On February 4, 1958, Raymond Glendore Bingham, M.R.C.S., L.R.C.P., formerly of The Garden House, Limes Avenue, Alfreton, Derby.
**Brodie.**—On January 12, 1958, at Blackpool, Lancs, Norman Brodie, M.R.C.S., L.R.C.P.
**Conlin.**—On February 4, 1958, at Middlesbrough, Yorks, Arthur Joseph Conlin, M.B., B.Ch.
**Dewar.**—On February 3, 1958, at the General Hospital, Nottingham, Allan Dewar, M.R.C.S., L.R.C.P., aged 74.
**Johnstone.**—On February 5, 1958, at Needwood Lodge, Rangemore, John Eccles St. George Johnstone, M.B., B.Ch., aged 84.
**Loewenstein.**—On February 7, 1958, Joseph Loewenstein, M.D., of 80, Green Hill, Hampstead, London, N.W.
**McKail.**—On February 4, 1958, at Harrow, Middx, David McKail, M.D., F.R.F.P.S., D.P.H., late of Glasgow, aged 83.
**MacMahon.**—On February 8, 1958, at Branksome Manor, The Avenue, Branksome Park, Bournemouth, John Ross MacMahon, M.B., C.M.
**Moore.**—On January 26, 1958, at the South London Hospital for Women, Florence Irene Rebecca Moore, M.B., B.S., of 6, Thurlow Road, Hampstead, London, N.W., aged 57.
**Nicoll.**—On January 26, 1958, at 48, Parkstone Avenue, Hornchurch, Essex, Robert Nicoll, M.B., Ch.B., of 104, Harley Street, London, W.
**Niven.**—On February 7, 1958, at 40, Whitgift Avenue, Croydon, Surrey, Adam Stephen Niven, M.D.
**Pegg.**—On February 1, 1958, in a nursing-home, John Henry Pegg, M.R.C.S., L.R.C.P., of 26, London Road, Reigate, Surrey, aged 87.
**Pritchett.**—On January 26, 1958, George William Morris Pritchett, M.R.C.S., L.R.C.P., of Garden Close, Poplar Grove, Woking, Surrey, late of Knaphill, Surrey.
**Rauchwerger.**—On January 26, 1958, Leon Rauchwerger, M.D., of Sudbury, Middlesex, aged 78.
**Stansfeld.**—On January 28, 1958, at Brocklesbury, Vicarage Lane, East Preston, Littlehampton, Sussex, Rex Stansfeld, *M.C.*, B.Chir., aged 69.
**Taylor.**—On February 5, 1958, Charles Leo Taylor, B.M., B.Ch., of Sudbury Town, Middx.

# Any Questions?

*We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.*

### Fitness for Diving

**Q.**—*Are there any specific medical tests that should be applied in selecting men for diving or for work in caissons? What conditions constitute a bar to selection?*

**A.**—In spite of the highly specialized nature of their calling, there are few specific tests of undisputed value in the selection of divers and caisson workers. A general clinical examination such as would be carried out for life assurance or entry to the armed Forces gives most of the information needed, but special attention should be paid to the ear, nose, and throat and respiratory systems.

Candidates for work under high pressure must be able to "clear their ears"—that is, be able to carry out a voluntary muscular movement which allows air to pass through the Eustachian tube and so equalize the pressure on either side of the ear-drum during rapid increases in the ambient pressure. Ability to perform this manœuvre is indicated by an intact and mobile ear-drum and a positive Valsalva test.

Doubtful cases should be submitted to a test dive in a compression chamber if such is available. This test serves the further purpose of helping to weed out individuals who are emotionally unsuited to the work and unlikely to tolerate the psychological stresses attendant on it. A reasonable assessment of pulmonary function is obtained by measuring the vital capacity, supplemented, of course, by clinical and *x*-ray examination of the chest. The vital capacity should not be less than 3.5 litres.

The main disqualifying conditions are those which interfere with "ear clearing," such as chronic disease of the middle ear, Eustachian tube, nose, and nasopharynx, and chronic diseases of the chest, such as emphysema and tuberculosis (including healed and quiescent cases), which diminish the amount of lung tissue available for gaseous exchange. Other conditions which constitute a bar to selection are skeletal and arthritic deformities, chronic skin disease, and a history of a thoracic or cranial operation. Hernia, extensive varicose veins, and haemorrhoids also disqualify unless successfully treated.

### Renal Function after Unilateral Nephrectomy

**Q.**—*Are renal function tests usually normal following a unilateral nephrectomy, and if they are not can it be taken that the remaining kidney must be diseased?*

**A.**—There is no simple answer to this question, because few experiments in man have been done where renal function has been assessed before removal of one abnormal kidney. Evidence from dog experiments suggests that within two or three months the remaining kidney will hypertrophy and be equal post-operatively to two normal kidneys. There is an increase in renal blood flow and glomerular infiltration rate, and renal function returns to normal. One would expect that in man the same occurs and that these exact parameters of renal function would be within normal limits some months after unilateral nephrectomy.

### Vaccination after Contact

**Q.**—*Does vaccination after contact with smallpox prevent or modify the disease?*

**A.**—The incubation period of smallpox is about twelve days. Detectable antibodies begin to appear in the blood three or four days after vaccination. There is abundant evidence that vaccination after contact may either prevent the disease or modify it, making it considerably milder. It is probably very significant that there have been no major outbreaks of smallpox in this country for many years past although the disease is introduced once, or more frequently, in practically every year. The immunity of the population as a whole is probably not very high, and it is most probable that the current policy of vaccinating contacts as soon as possible is responsible for our freedom from the disease.

### Size of Lumbar Puncture Needles

**Q.**—*What size of lumbar puncture needle is advised for use in different age groups? Presumably an unnecessarily thin needle increases the likelihood of breakage, but are there any disadvantages in using a stout needle?*

**A.**—Two sizes of lumbar puncture needle are commonly used at the National Hospital for Nervous Diseases, Queen Square, London. For adults, either a Greenfield needle of 5 in. (12.7 cm.) or a Harris needle of 4½ in. (11.5 cm.), both of 19 gauge, is used, and for children a Greenfield needle of 20 gauge.

The question implies that risk of damage or breakage is likely, and related to the amount of force needed to perform the puncture. It is most important to realize that only gentle pressure should ever be used during the puncture. As soon as resistance is felt the needle must be withdrawn and used along a new track. No attempt should ever be made to overcome resistance by force. The operator is seeking for a soft-tissue pathway. If there is local bone disease, causing a bone barrier, lumbar puncture should not be attempted. A sample of spinal fluid might be obtained by cisternal puncture. If the patient is restless, he should either be so securely held that he cannot, by a sudden movement, damage himself or the needle or be under brief general anaesthesia.

The disadvantage of a fine needle is that only a very slow flow of fluid may be obtained. The disadvantages of a stout needle are, first, that slightly more trauma results in the tissues of the back; secondly, and more serious, the risk of too sudden and profuse a flow of fluid should the intracranial pressure be high (a strong contraindication to lumbar puncture anyway); and, thirdly, the larger the hole in the spinal theca, the greater the risk of escape of cerebrospinal fluid into the perithecal tissues, which is often accompanied by severe low-pressure headache.

### Systolic Blood Pressure

**Q.**—*Which method of sphygmomanometry—auscultatory, palpatory, or oscillatory—gives the most accurate value for the systolic blood pressure? What in each case should be taken as the "end point," and what is the significance of the small oscillations in the mercury or aneroid sphygmomanometer that occur just before the systolic sounds become audible? Do they reflect the systolic level more accurately than the sounds?*

**A.**—To some extent the answer is dependent on the sensibility of the ears, fingers, and eyes of the observer. Most find the auscultatory method the most satisfactory. The end point for the several methods respectively is the first appearance of the sounds over the brachial artery, the first pulse beat felt at the wrist, and an abrupt increase in the size of the oscillations.

The small oscillations in the mercury occurring before the end point for the systolic pressure are due to the pulsation of the brachial artery deforming the upper edge of the cuff, which acts in this way rather like a plethysmograph.

### Prophylaxis for Tinea Pedis

**Q.**—*What prophylactic measures are advisable against tinea pedis in shower-baths recently installed in an iron foundry?*

**A.**—Fungous infection of the feet in those using shower-baths results from their picking up fragments of infected scales which have been deposited on the floor from the feet of previous users. This can be prevented only by adopting

one of the following procedures. Each bather should have his own slippers, which he should wear in the shower-bath; this prevents deposition and picking up of scales. The feet may be washed separately at a foot trough with running water and without resting the feet on the floor of the trough. Alternatively the floor of the shower-bath should be thoroughly scrubbed and swilled down after each usage. The use of fungicides here is of doubtful value; it is the mechanical cleansing that is necessary. Other points are that the feet should be carefully dried and dusted with a foot powder. The co-operation of the employees should be obtained by explaining the reason for these procedures.

### Mastication and Digestion

**Q.**—*Is there any evidence that incomplete mastication causes inefficient digestion?*

**A.**—There is no evidence that incomplete mastication leads to inefficient digestion. Edentulous patients, however, often avoid eating such food as meat and fresh fruit, and their nutrition may suffer in consequence. Unless there is evidence that they are not getting a sufficiently varied diet, there does not seem to be any medical justification for persuading old patients to wear dentures if they are more comfortable without them.

### Phenylbutazone with Steroid Therapy

**Q.**—*Is there any objection to combining phenylbutazone with steroid therapy in the treatment of rheumatoid arthritis? If not, what dosage schedule is advised?*

**A.**—The majority of investigators have not combined phenylbutazone with steroid therapy, because they wish to study the effect of one drug only in the management of rheumatoid arthritis. The theoretical disadvantage of combining these two drugs is that each has a tendency to produce peptic ulceration, and therefore they might have an additive effect when used together. The dose of prednisone or prednisolone for prolonged oral therapy should not be above 15 mg. a day, and that of cortisone not above 75 mg. a day. Phenylbutazone can be given for short periods in a dose of 600 mg. a day, but should be reduced to 400 mg. a day before long.

### Cortisone in Pregnancy

**Q.**—*What is the steroid of choice to use in a pregnant woman with disseminated lupus erythematosus, now on cortisone? What are possible complications in such a case, and are there any special dangers to the child?*

**A.**—A review of the literature would not suggest that continued administration of cortisone throughout pregnancy carries any significant risk to either mother or child, apart from the well-known side-effects of cortisone itself. In a woman with disseminated lupus erythematosus who is well maintained on cortisone it would probably be unwise to shift to any other steroid unless certain clear-cut indications arose, such as a rapid increase in weight due to fluid retention. In this event transfer to prednisone or prednisolone would be advisable, the dose used being initially one-quarter of the maintenance dose of cortisone, with subsequent adjustment if necessary. With prednisone or prednisolone it is unwise for the maintenance dose to be above 10 mg. daily.

### Combined Malaria and Amoebiasis Prophylaxis

**Q.**—*Is one daily tablet of "nivembin," containing the equivalent of 50 mg. chloroquine base with 300 mg. di-iodohydroxyquinoline, an effective prophylactic against malaria and amoebiasis? Is there any risk of inducing drug-resistant amoebae or malarial parasites?*

**A.**—Prophylaxis against malaria with this dosage of chloroquine should be perfectly satisfactory, but the value of the given amount of di-iodohydroxyquinoline is as yet completely unproved. There is no risk of inducing drug-resistant malarial parasites, but this possibility cannot be excluded in the case of amoebic parasites. The use of the prophylactic against amoebic infection is open to criticism for this reason, and also because it might mask an infection, which would thereby be unrecognized and quite possibly give rise to hepatic or other complications.

## NOTES AND COMMENTS

**Intestinal Moniliasis.**—Mr. P. A. SHEPHERD (chief bacteriologist, Aplin and Barrett Ltd., Yeovil) writes: With reference to the answer given to the question on the above subject ("Any Questions?" January 18, p. 173), may I be permitted to draw attention to a form of therapy which we are at the moment investigating, for the suppression of intestinal infections due to monilia and staphylococci following oral antibiotic therapy? There is evidence that antibiotics can give rise to monilial infections. Anderson[1] reports that oxytetracycline not only stimulates the growth of *Candida albicans* but may also increase its pathogenicity. Similar findings have also been reported by Pappenfort and Schnall,[2] Foley and Winter,[3] and Moore.[4] Young *et al.*[5] studying the effect of *Lactobacillus acidophilus* on the growth of *C. albicans*, came to the conclusion that a counterbalance existed between the two organisms. They state that the increase in *C. albicans* following antibiotic therapy results from the destruction of the normally inhibitory lactobacilli. This inhibition of *C. albicans* by lactobacilli is confirmed by Rosebury *et al.*[6] Following these reports we produced a preparation containing antibiotic-resistant strains of *L. acidophilus* for oral administration during antibiotic therapy to prevent superinfections by staphylococci and monilia. This preparation has so far proved satisfactory for its purpose for both the suppression and elimination of monilia[7] and the suppression of staphylococci.[8]

REFERENCES

1 Anderson, T., *Practitioner*, 1956, **176**, 24.
2 Pappenfort, R. B., and Schnall, E. S., *Arch. intern. Med.*, 1951, **88**, 729.
3 Foley, G. E., and Winter, W. D., *J. infect. Dis.*, 1949, **85**, 2-8.
4 Moore, M., *J. Lab. clin. Med.*, 1951, **37**, 703.
5 Young, G., Krasner, R. I., and Yudkofsky, P. L., *J. Bact.*, 1956, **72**, 525.
6 Rosebury, T., Gale, D., and Taylor, D. F., ibid., 1954, **67**, 135.
7 Marget, W., Medizinische Gesellschaft Freiburg i/Br., November 27, 1956.
8 Gordon, D., Macrae, J., and Wheater, D. M., *Lancet*, 1957, **1**, 899.

**Hot-air Sterilization.**—Dr. N. PINES (London, N.W.11) writes: With reference to hot-air sterilization ("Any Questions?" January 25, p. 236), in 1912 I was for a time a clinical assistant to Dr. Gallemaerts, professor of ophthalmology in Brussels. All instruments for intraocular operations, including cataract knives, were cleaned in hot water and soap, and after drying put in a special hermetically closed metallic box, together with a capsule containing crystals of salicylic acid and methyl violet. Salicylic acid melted at a temperature of 160° C. and the contents became coloured, so testifying that the necessary temperature was reached inside the box.

**Collected Articles from the "British Medical Journal"**

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

*Emergencies in General Practice* (26s. 9d.).

*Refresher Course for General Practitioners*, Volumes 2 and 3 (26s. 9d.).

*Clinical Pathology in General Practice* (22s. 3d.).

*Any Questions?*, Volumes 2 and 3 (8s. 3d. each).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecret, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.